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TITLE OF THE INVENTION (500 characters max)

CHIMPANZEE ADENOVIRUS VACCINE CARRIERS

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CHIMPANZEE ADENOVIRAL VACCINE CARRIERS

FIELD OF THE INVENTION

The present invention relates to the field of recombinant vectors and more specifically to the production and use of recombinant replication-defective chimpanzee adenoviral vectors to elicit immune responses in mammalian hosts.

BACKGROUND OF THE INVENTION

The adenoviruses (Ads) comprise a large family of double-stranded DNA viruses found in amphibians, avians, and mammals which have genome organization and a nonenveloped icosahedral capsid structure (Straus, Adenovirus infections in humans. In *The Adenoviruses.* 451-498, 1984; Hierholzer *et al., J. Infect. Dis., 158*: 804-813, 1988; Schnurr and Dondero, *Intervirology., 36*: 79-83, 1993; Jong *et al., J Clin Microbiol., 37*:3940-3945:1999). In contrast to retroviruses, adenoviruses can transduce numerous cell types of several mammalian species, including both dividing and nondividing cells, without integrating into the genome of the host cell.

Generally speaking, adenoviral DNA is typically very stable and remains episomal (e.g., extrachromosomal), unless transformation or tumorigenesis has occurred. In addition, adenoviral vectors can be propagated to high yields in well-defined production systems which are readily amenable to pharmaceutical scale production of clinical grade compositions. These characteristics and their well-characterized molecular genetics make recombinant adenoviral vectors good candidates for use as vaccine carriers. Typically, the production of recombinant adenoviral vectors relies on the use of a packaging cell line which is capable of complementing the functions of adenoviral gene products that have been either deleted or engineered to be nonfunctional.

Presently, two well-characterized human subgroup C adenovirus serotypes (i.e., hAd2 and hAd5) are widely used as the sources of the viral backbone for most of the adenoviral vectors that are used for gene therapy. Replication-defective human adenoviral vectors have also been tested as vaccine carriers for the delivery of a variety of immunogens derived from a variety of infectious agents (e.g., viruses, parasites, or bacterial pathogens) and tumor cells, including tumor-associated antigens (TAAs). Studies conducted in experimental animals (e.g., rodents, canines and nonhuman primates) indicate that recombinant replication-defective human adenoviral vectors carrying transgenes encoding immunogens derived from the E6 and E7 oncoproteins of human papillomavirus (HPV-16) (He, Z *et al.*, (2001) *Virology*, 270:3583-3590,

the rabies virus glycoprotein (Xiang, Z. *et al* (1996) Virolgy, 219:220-227), the circumsporozoite protein of *Plasmodium falciparum* Rodriguez, E. *et al.* (1997) *J. Immunol.* 158:1268-1274) as well as other heterologous antigens elicit both humoral and cell-mediated immune responses against the transgene product. Generally speaking, investigators have reported success using human adenoviral vectors as vaccine carriers in nonhuman experimental systems by either using an immunization protocols that utilizes high doses of recombinant adenoviral vectors that are predicted to elicit immune responses; or by using immunization protocols which employ the sequential administration of adenoviral vectors that are derived from different serotypes but which carry the same transgene product as boosting immunizations (Mastrangeli, *et al., Human Gene Therapy*, 7: 79-87 (1996).

However, it is predicted that vaccine carriers derived from ubiquitous human serotypes, such as types 2 and 5, will encounter preexisting humoral and cellular immunity in the human population. Thus, although replication-defective recombinant human adenoviruses have been successfully employed as vaccine carriers in experimental systems employing rodent, canine, and nonhuman primate hosts; human innate and adaptive immunity is expected to significantly limit the utility of these serotypes as vaccine carriers. This expectation is based on the fact that subgroup C, which includes type 2 and type 5, adenoviral infection is endemic in the human population. As a consequence, the majority of humans seroconvert within the first five years of life as the result of a natural infection.. Thus, vectors derived from viruses that naturally infect and replicate in humans may not be optimal candidates for use as vaccine carriers.

Another problem associated with the use of human adenoviral-derived vectors is the risk that the production method used to propagate the recombinant viruses will give rise to vector stocks that are contaminated with replication competent adenovirus (RCA). This is caused by homologous recombination between overlapping sequences from the recombinant vector and the adenoviral genes that are present in the E1-complementing helper cell lines such as human 293 (Graham, F.L. *et al,* (1977) *J. Gen. Virol.* 36:59-72.) cells. The presence of RCA in vector stocks prepared for use in clinical trials constitutes a safety risk because it can promote the mobilization and spread of the replication defective virus. Spread of the defective virus can aggravate the host immune response and cause other adverse immunopathological consequences (Fallux, F. J., *et al.* Human Gene Therapy 9: 1909-1917 (1998). Accordingly, the Food and Drug Administration (FDA) and other regulatory bodies have promulgated guidelines which establish limits on the levels of RCA that can be present in vector preparations intended for clinical use. The intent of imposing RCA limits is to ensure limited exposure of patients to replicating adenovirus in compositions that are used in clinical trials.

Thus, there continues to be a need for the development of adenoviral vaccine carriers that are suitable for use in mammalian hosts which are: easy to manipulate, amenable to pharmaceutical scale production and long term storage, capable of high-level replication in human complementation cell lines, highly immunogenic, devoid of neutralizing B cell epitopes that cross-react with the common serotypes of human adenoviruses, comply with the safety RCA standards promulgated by regulatory agencies, and which are amenable for use in prime/boost protocols that are suitable for use in humans.

SUMMARY OF THE INVENTION

The present invention relates to recombinant replication-defective adenovirus vectors derived from chimpanzee adenoviruses and methods for generating chimpanzee adenoviral vectors in human E1-expressing cell lines. The invention also provides methods for generating clinical grade vector stocks suitable for use in humans and means for using the disclosed vectors as vaccine carriers to elicit protective and/or therapeutic immune responses. The invention further provides methods for using the recombinant adenoviruses of the invention to prepare vaccine compositions designed to delivery, and direct the expression of, transgenes encoding immunogens. In one embodiment, the invention contemplates the use of the disclosed vectors as vaccine carriers for the administration of vaccines comprising transgenes encoding immunogens derived from an infectious agent. In a second embodiment, the invention contemplates the use of the disclosed vectors to prepare and administer cancer vaccines. In a particular embodiment, the invention contemplates the preparation and administration of a cancer vaccine comprising a transgene encoding a TAA.

In one aspect, the invention discloses the complete genomic sequence of five chimpanzee adenoviruses (ChAds), referred to herein as ChAd3 (SEQ ID NO: 1) (Figures 5A-5V), ChAd6 (SEQ ID NO: 2) (Figures 6A-6V, CV32 (SEQ ID NO:3) (Figures 7A-7K), CV33 (SEQ ID NO: 4) (Figures 8A-8K), and CV23 (SEQ ID NO:5) (Figures 9A-9J). ChAd3 and ChAd6 represent novel adenoviruses isolated according to the methods disclosed herein. The genomes of the ChAd3 and ChAd6 are 37741 and 36648 base pairs in length, respectively. ChAd3 hexon gene is comprised between nt 19086-21968(SEQ ID NO: 41) while fiber gene is comprised between nt 32805-34490 (SEQ ID NO: 42). ChAd6 hexon gene is comprised between nt 18266-21127 (SEQ ID NO: 43)while fiber gene is comprised between nt 32218-33555 (SEQ ID NO: 44). .Based on sequence homology deduced from a multiple sequence alignment of full-length hexon peptides, ChAd3 has been classified into human subgroup C and ChAd6 has been classified into human subgroup E.

The genomes of the CV32, CV33 and CV23 adenoviruses are 36,606, 36,535, and 32,020 base pairs in length, respectively. CV32 (Pan 6, ATCC N. VR-592), CV33 (Pan 7, ATCC N. VR-593) and CV23 (Pan 5) (Esoterix Inc.,) have all been determined to be related to human Ad4 (hAd4) (subgroup E) (Wigand, R *et al. Intervirology* 1989, 30:1-9). However, based on hexon sequence alignment CV32 has subsequently characterized as being more closely analogous to human subgroup D members than to hAd4.

In a second aspect, the invention provides nucleotide sequences for the fiber and hexon genes of ten additional chimpanzee adenoviruses (ChAd20, ChAd4, ChAd5, ChAd7, ChAd9, ChAd10, ChAd11, ChAd16, ChAd17 and ChAd19) isolated according to the methods disclosed herein. The fiber gene sequences are set forth in Figures 10-19 and SEQ ID NOS: 6-15: (SEQ ID NO: 6, ChAd20); (SEQ ID NO: 7, ChAd4); (SEQ ID NO: 8, ChAd5); (SEQ ID NO: 9, ChAd7); (SEQ ID NO: 10, ChAd9); (SEQ ID NO: 11, ChAd10); (SEQ ID NO: 12, ChAd11); (SEQ ID NO: 13, ChAd16) (SEQ ID NO: 14, ChAd17) and (SEQ ID NO: 15, ChAd19). Figures 20A-20D provides a comparison of the amino acid sequences of the fiber proteins disclosed and claimed herein.

The hexon gene sequences are set forth in Figures 21-30 and SEQ ID NOS: 16-25: (SEQ ID NO: 16, ChAd20); (SEQ ID NO: 17, ChAd4); (SEQ ID NO: 18, ChAd5); (SEQ ID NO: 19, ChAd7); (SEQ ID NO: 20, ChAd9); (SEQ ID NO: 21, ChAd10); (SEQ ID NO: 22, ChAd11); (SEQ ID NO: 23, ChAd16); (SEQ ID NO: 24, ChAd17) and (SEQ ID NO: 25; ChAd19). Figures 31A-31M provide a comparison of the amino acid sequences of the hexon proteins disclosed and claimed herein. A multiple sequence alignment of hexon proteins allows an artisan to perform a phylogenetic analysis of that is consistent with the proposed classification of human adenoviral serotypes (Rux, J.J., *et al* (2003) J. Virol. 77:9553-9566).

In an alternative aspect, the invention further provides ten additional chimpanzee adenovirus isolates. Samples comprising ChAd20, ChAd4, ChAd5, ChAd7, ChAd9, ChAd10, ChAd11, ChAd16, ChAd17 and ChAd19 were deposited on December 12, 2003 with the European Collection of Cell Cultures (ECACC, Porton Down, Salisbury, Wiltshire, SP4 0JG, United Kingdom) as an original deposit under the Budapest Treaty. The deposits were assigned accession numbers: 03121201 (ChAd4), 03121202 (ChAd5) , 03121203 (ChAd7) , 03121204 (ChAd9) , 03121205 (ChAd10), 03121206 (ChAd11), 03121207 (ChAd16), 03121208 (ChAd17), 03121209 (ChAd19) and 03121210 (ChAd20) . These deposits will be maintained under the terms of the *Budapest Treaty* on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. These deposits were made merely as a convenience for those of skill in the art and are not an admission that a deposit is required under 35 U.S.C. §112. All restrictions on the availability to the public of the deposited material will be

irrevocably removed, except for the requirements specified in 37 C.F.R. §1.808(b), upon the granting of a patent.

In a third aspect, the invention provides replication-defective recombinant adenoviral vectors which are capable of infecting mammalian cells, preferably human cells, and directing expression of encoded transgene product(s). As demonstrated herein, the disclosed vectors are suitable for use as vaccine carriers for the delivery of transgenes comprising immunogens against which an immune response is desired. In particular embodiments, the invention provides recombinant replication-defective chimpanzee adenoviral vectors that are capable of high-level replication in human E1-expressing (i.e., packaging) cell lines. In one embodiment, the invention provides recombinant adenoviruses that are capable of replicating in PER.C6™ cells.

Generally speaking, the recombinant vectors encompassed by the invention provide vaccine carriers that will evade pre-existing immunity to the adenovirus serotypes that are typically encountered in the human population. More specifically, the recombinant vectors of the invention comprise vector backbone sequences which are shown herein to be devoid of neutralizing B epitopes that cross-react with the common serotypes of human adenoviral derived vectors.

The invention further provides group-specific shuttle vectors that include an adenoviral portion and a plasmid portion, wherein said adenoviral portion generally comprises: a) viral left end (ITR and packaging signal), part of the pIX gene and viral genome right end; and b) a gene expression cassette. The group-specific shuttle vectors are designed to exploit the nucleotide sequence homology which is observed between adenoviruses that are assigned to the same serotype subgroup (i.e., subgroups A, B, C, D or E), and can be used to manipulate the nucleotide sequences disclosed herein and/or to clone other chimpanzee adenoviruses belonging to the same subgroup generating an adenovirus pre-plasmid containing a chimp adenoviral genome deleted of E1 region.

Other aspects of this invention include host cells comprising the adenoviral vaccine vectors and/or the adenovirus pre-plasmid vectors, methods of producing the vectors comprising introducing the adenoviral vaccine vector into a host cell which expresses adenoviral E1 protein, and harvesting the resultant adenoviral vaccine vectors. In a particular embodiment, the invention provides a method of producing a replication-defective chimpanzee adenoviral vector comprising introducing one of the disclosed adenoviral vectors into an adenoviral E-1 expressing human cell, and harvesting the resulting recombinant adenoviruses.

Another aspect of the invention also provides vaccine compositions which comprise an adenoviral vector of the invention. Compositions comprising recombinant

chimpanzee adenoviral vectors may be administered alone or in combination with other viral- or non-viral-based DNA/protein vaccines. They also may be administered as part of a broader treatment regimen. These compositions can be administered to mammalian hosts, preferably human hosts, in either a prophylactic or therapeutic setting. As shown herein, administration of the disclosed vaccine compositions, either alone or in a combined modality, such as a prime boost regimen or multiple injections of serologically distinct Ad vectors results in the induction of an immune response in a mammal that is capable of specifically recognizing the immunogen encoded by the transgene.

One of the methods disclosed and claimed herein, comprises administering to a mammal (that is either naïve or primed to be immunoreactive to a target antigen), a sufficient amount of a recombinant chimpanzee adenoviral vector, containing at least a functional deletion of its wild-type E1 gene, carrying a sequence comprising a promoter capable of directing expression of a nucleotide sequence encoding the least one target antigen, wherein administration of the recombinant vector elicits (or primes) an antigen-specific immune response.

In one embodiment, the invention provide a method designed to induce an immune response (prophylactic or therapeutic) against an infectious agent (e.g., a viral or bacterial pathogen or a mammalian parasite). In a second embodiment, the invention provides a method designed to induce an immune response in a mammal that will break tolerance to a self-antigen, such as a TAA. This aspect of the invention contemplates the use of the disclosed vectors as a vaccine carrier for the preparation and administration of cancer vaccines.

Yet other embodiments and advantages of the present invention will be readily apparent from the following detailed description of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic drawing which summarizes the cloning strategy used to construct a ChAd6 shuttle vector (pARS ChAd6-3).

Figure 2 is a schematic drawing which illustrates the cloning strategy used to clone the ChAd6 viral genome by homologous recombination in *E.coli* strain BJ5183.

Figure 3 is a schematic drawing illustrating the elements of various ChAd6 shuttle plasmids including: pARS ChAd6-3 GAG; pARS ChAd6-3 SEAP; pARS ChAd6-3 EGFP; and pARS ChAd6-3 NS MUT.

Figure 4 is a schematic drawing which illustrates the homologous recombination scheme utilized to clone the ChAd6 ΔE1expression vectors.

Figures 5A-5V provides the genomic nucleotide sequence of ChAd3 (SEQ ID NO: 1).

Figures 6A-6V provides the genomic nucleotide sequence of ChAd6 (SEQ ID NO: 2).

Figures 7A-7K provides the genomic nucelotide sequence of CV32 (SEQ ID NO: 3).

Figures 8A-8K provides the genomic nucleotide sequence of CV33 (SEQ ID NO: 4).

Figures 9A-9J provides the genomic nucleotide sequence of CV23 (SEQ ID NO: 5).

FigureS 10 A and B provides the nucleotide sequence of the fiber gene of ChAd20 (SEQ ID NO: 6).

Figures 11 A and B provides the nucleotide sequence of the fiber gene of ChAd4 (SEQ ID NO: 7).

Figures 12 A and B provides the nucleotide sequence of the fiber gene of ChAd5 (SEQ ID NO: 8).

Figures 13 A and B provides the nucleotide sequence of the fiber gene of ChAd7 (SEQ ID NO: 9).

Figures 14 A and B provides the nucleotide sequence of the fiber gene of ChAd9 (SEQ ID NO: 10).

Figures 15 A and B provides the nucleotide sequence of the fiber gene of ChAd10 (SEQ ID NO: 11).

Figures 16 A and B provides the nucleotide sequence of the fiber gene of ChAd11 (SEQ ID NO: 12).

Figures 17 A and B provides the nucleotide sequence of the fiber gene of ChAd16 (SEQ ID NO: 13).

Figures 18 A and B provides the nucleotide sequence of the fiber gene of ChAd17 (SEQ ID NO: 14).

Figures 19 A and B provides the nucleotide sequence of the fiber gene of ChAd19 (SEQ ID NO: 15).

Figures 20A-20D provides a comparison of the amino acid sequences of the fiber proteins of C1, ChAd11, ChAd20, ChAd17, ChAd3, ChAd19, PAN6, ChAd5, ChAd6, ChAd7, PAN5, PAN7, ChAd9, ChAd10, ChAd4, CV68 and ChAd16.

Figures 21A-21C provides the nucleotide sequence of the hexon gene of ChAd20 (SEQ ID NO: 16).

Figures 22A-22C provides the nucleotide sequence of the hexon gene of ChAd4 (SEQ ID NO: 17).

Figures 23A-23C provides the nucleotide sequence of the hexon gene of ChAd5 (SEQ ID NO: 18).

Figures 24A-24C provides the nucleotide sequence of the hexon gene of ChAd7 (SEQ ID NO: 19).

Figures 25A-25C provides the nucleotide sequence of the hexon gene of ChAd9 (SEQ ID NO: 20).

Figures 26A-26C provides the nucleotide sequence of the hexon gene of ChAd10 (SEQ ID NO: 21).

Figures 27A-27C provides the nucleotide sequence of the hexon gene of ChAd11 (SEQ ID NO: 22).

Figures 28A-28C provides the nucleotide sequence of the hexon gene of ChAd16 (SEQ ID NO: 23).

Figures 29A-29C provides the nucleotide sequence of the hexon gene of ChAd17 (SEQ ID NO: 24).

Figures 30A-30C provides the nucleotide sequence of the hexon gene of ChAd19 (SEQ ID NO: 25).

Figures 31A-31M provides a comparison of the amino acid sequences of the hexon proteins of : hAd12, hAd3, hAd7, hAd11, hAd21, hAd34, hAd35, C1, hAd1, hAd2, hAd5, ChAd3, ChAd11, ChAd17, ChAd19, ChAd20, hAd48, ChAd4, ChAd5 ChAd7, ChAd16, Pan6, hAd4, hAd16, ChAd6, ChAd9, ChAd10, C68, Pan5, Pan7, hAd41 and hAd40.

Figure 32 provides a listing of the oligonucleotide sequences (SEQ ID NOS: 26-46) disclosed herein.

Figure 33 is a graphic representation of the immunization break-point of ChAd vectors belonging to different serotype subgroups (i.e., subgroups C, E and D). The lowest dose eliciting a measurable immune response was determined by performing titration experiments in mice immunized with gag-expressing ChAd3, ChAd11, ChAd20, CV33, CV68, ChAd6, ChAd9, ChAd10, CV32, ChAd4, ChAd7 and ChAd16 vectors.

Figure 34 provides a graphic representation of a CEA-specific T cell response elicited in rhesus macaques immunized sequentially with a human adenoviral vector (MRKAd5 RhCEA) followed by a chimpanzee adenoviral vector (CV33 RhCEA) after 12 week interval. The immune responses were evaluated by IFN-γ ELISPOT assay, and the data illustrate the number of spot-forming cells (SFC) per million peripheral blood mononuclear cells (PBMC)

following incubuation in the absence (DMSO) and presence of rhesus CEA C and D peptide pools.

Figure 35 provides a phylogenetic tree of human and chimpanzee adenoviruses of deduced from a multiple sequence alignment of full-length hexon peptide sequences using PAUPSEARCH (Wisconsin Package Version 10.3, Accelrys Inc.) and visualized and manipulated with TREEVIEW.

Figure 36 is a graphic representation of immunization results obtained in response to the administration of ChAd3 and hAd5 gag vectors to mice which were pre-exposed to hAd5. Cell-mediated immunity was evaluated 3 weeks post-immunization by IFN-γ ELISPOT using purified splenocytes.

Figure 37 is a graphic representation of kinetics of anti-CEA CMI elicited in human CEA transgenic mice immunized with ChAd3hCEA and Ad5hCEA. CMI was evaluated by ICS of PBMC stimulated with CEA peptide pool. The results are expressed as % of $IFN\gamma^+$ $CD8^+$/total PBMC.

DETAILED DESCRIPTION OF THE INVENTION

As used throughout the specification and appended claims, the following definitions and abbreviations apply:

The term "cassette" refers to a nucleic acid molecule which comprises at least one nucleic acid sequence that is to be expressed, along with its transcription and translational control sequences. Changing the cassette, will cause the vector into which is incorporated to direct the expression of different sequence or combination of sequences. In the context of the present invention, the nucleic acid sequences present in the cassette will usually encode an immunogen. Because of the restriction sites engineered to be present at the 5' and 3' ends, the cassette can be easily inserted, removed or replaced with another cassette.

The term "*cis*-acting element" refers to nucleotide sequences which regulate genes to which they are attached. *Cis*-acting elements present in DNA regulate transcription, and those transcribed into mRNA can regulate RNA processing, turnover and protein synthesis.

The term "vector" refers to some means by which DNA fragments can be introduced into a host organism or host tissue. There are various types of vectors including plasmid, virus (including adenovirus), bacteriophages and cosmids.

The term "promoter" refers to a recognition site on a DNA strand to which an RNA polymerase binds. The promoter forms an initiation complex with RNA polymerase to

initiate and drive transcriptional activity. The complex can be modified by activating sequences such as enhancers, or inhibiting sequences such as silencers.

The term "pharmaceutically effective amount" refers to an amount of recombinant adenovirus that is effective in a particular route of administration to transduce host cells and provide sufficient levels of transgene expression to elicit an immune response.

The term "replication-competent" recombinant adenovirus (AdV) refers to an adenovirus with intact or functional essential early genes (i.e., E1A, E1B, E2A, E2B and E4). Wild type adenoviruses are replication competent.

The term "replication-defective" recombinant AdV refers to an adenovirus that has been rendered to be incapable of replication because it has been engineered to have at least a functional deletion, or a complete removal of, a gene product that is essential for viral replication. The recombinant chimpanzee adenoviral vectors of the invention are replication-defective.

The term "mammalian" refers to any mammal, including a human being.

The term "percent sequence identity" or "identical" in the context of nucleic acid sequences refers to the residues in the two sequences that are the same when aligned for maximum correspondence. The length of sequence identity comparison may be over the full-length of the genome. (e.g., about 36 kbp), the full-length of an open reading frame of a gene, protein, subunit, or enzyme [see, e.g., the tables providing the adenoviral coding regions], or a fragment of at least about 500 to 5000 nucleotides, is desired. However, identity among smaller fragments, e.g. of at least about nine nucleotides, usually at least about 20 to 24 nucleotides, at least about 28 to 32 nucleotides, at least about 36 or more nucleotides, may also be desired. Similarly, "percent sequence identity" may be readily determined for amino acid sequences, over the full-length of a protein, or a fragment thereof. Suitably, a fragment is at least about 8 amino acids in length, and may be up to about 700 amino acids. Examples of suitable fragments are described herein.

Identity is readily determined using such algorithms and computer programs as are defined herein at default settings. Preferably, such identity is over the full length of the protein, enzyme, subunit, or over a fragment of at least about 8 amino acids in length. However, identity may be based upon shorter regions, where suited to the use to which the identical gene product is being put.

In general, adenoviral constructs, gene constructs are named by reference to the genes contained therein. For example, "pChAd3 ΔE1gag" refers to a plasmid construct which comprises a ChAd3 chimpanzee adenoviral genome deleted of the E1 region. In this plasmid, the E1 region is replaced by an immunogen expression cassette comprising an HIV gag gene

under the control of a human CMV promoter followed by a bovine growth hormone polyadenylation signal. Similarly, pCV33DE1-E3 NSmut, refers to a second plasmid construct disclosed herein which comprises a CV33 chimpanzee adenoviral genome, deleted of the E1 and E3 regions, which is replaced by an immunogen expression cassette comprising HCV non-structural genes under the control a human CMV promoter followed by a bovine growth hormone polyadenylation signal.

The abbreviation "Ag" refers to an antigen.

As used throughout the specification and in the appended claims, the singular forms "a," "an," and "the" include the plural reference unless the context clearly dictates otherwise.

Adenoviruses (Ads) are noneveloped, icosahedral viruses that have been identified in several avian and mammalian hosts. Human Ads (hAd) belong to the Mastadenovirus genus which includes all known human and many Ads of animal (e.g., bovine, porcine, canine, murine, equine, simian and ovine) origin. Human adenoviruses are divided into six subgroups (A-F) based on a number of biological, chemical, immunological and structural criteria which include hemagglutination properties of rat and rhesus monkey erythrocytes, DNA homology, restriction enzyme cleavage patterns, percentage G+C content and oncogenicity (Straus, 1984, In *The Adenoviruses*, ed. H. Ginsberg, pps. 451-498, New York: Plenus Press, and Horwitz, 1990 In *Virology*, eds. B.N. Fields and D.M. Knipe, pps. 1679-1721). To date, 51 distinct serotypes have been recognized and grouped into subgroups on the basis of their hemagglutination properties and biophysical and biochemical criteria.

The adenoviral virion has an icosahedral symmetry and, depending on the serotype, a diameter of 60-90 nm. The icosahedral capsid consists three major proteins, hexon (II), penton base (III) and a knobbed fibre (IV) as well as a number of minor proteins (i.e., VI, VIII, IX, IIIa and IVa2) (W.C. Russel, *J. Gen. Virol.*, 81: 2573-2604 (2000). One aspect of the preexisting immunity that is observed in humans is humoral immunity, which can result in the production and persistence of antibodies that are specific for viral proteins. The humoral response elicited by adenovirus is mainly directed against the major structural proteins: hexon, penton and fiber.

Published reports have established that titers comprising antibodies against multiple serotypes are common (Dambrosio, E. (1982) *J. Hyg.* (London) 89: 209-219) and that a substantial portion of the preexisting titers have neutralizing activity. Neutralizing immunity to adenovirus is type specific, and infection with a particular serotype of adenovirus confers immunity only to that serotype. Several reports have suggested that antibodies directed towards the hexon are the strongest and the most neutralizing (Toogood, C.I.A., Crompton, J. and Hay

R.T. (1992) *J.Gen. Virol.* 73, 1429-1435). Therefore, it is reasonable to assume that the epitopes responsible for type-specific neutralization are located within seven hypervariable regions identified by alignment of the hexon sequences deriving from different serotypes. (Crawford-Miksza, L and D.P.Schnurr. (1996) *J.Virol.*70:1836-1844).

A direct correlation between the presence of type-specific neutralizing antibodies and the inability to elicit an immune response with a vector based on the same serotype has been established by different methods including the passive transfer of immune sera from treated to naïve animals. Generally speaking, preexisting humoral immunity for a specific viral serotype reduces the therapeutic efficacy of the vector administration. Moreover, the administration of a vector based on a specific viral serotype elicits an immune-response against the vector that prevents the re-administration of the same serotype.

In a particular embodiment, the invention provides a method of circumventing the adverse effects associated with the consequences of preexisting immunity to common serotypes of hAds. More specifically, the invention contemplates the use of chimpanzee adenoviral vectors characterized by a serotype that does not circulate in humans. Accordingly, the invention provides adenoviral (Chad) vectors which lack neutralizing B-cell epitopes that cross react with those of common human serotypes as a vaccine carrier.

Although it has been reported that adenoviral-specific cell mediated immunity (CMI) can be cross-reactive, vaccination studies based on repeated injections of multiple serotypes demonstrated a higher efficiency than immunization schedules based on a single vector. These experiments further demonstrate that the main limitation of a vector administration for vaccine purposes is the humoral pre-existing immunity against the vector. Potential solutions to the problems associated with the use of a human adenovirus as a vaccine carrier include the administration of a higher dose of an adenovirus (e.g., a subgroup C serotype) that is predicted to encounter a preexisting immune response, and the use of vectors based on rare human serotypes. However, the use of higher doses of vaccine increases the cost of the vaccine and risk of undesirable side effects and the results of preclinical testing suggest that human alternate serotypes are less immunogenic than hAd5 and hAd6.

In an attempt to avoid the problems of host humoral and cellular immune responses against the adenoviral backbone elements of the vector, and to minimize the risk of using human adenovirus-derived vector stocks that may be contaminated with replication-competent adenoviruses (RCA), several nonhuman adenoviruses have been characterized and developed as vaccine carriers (Soudois, C. *et al* (2000) *J. Virology*, 74:10639-10649; Farina, S.F. *et al* (2001) *J. Virology*, 75:11603-11613; Cohen, C.J. *et al* (2002) *J. Gen. Virology*, 83:151-155.) The premise underlying the use of nonhuman adenoviral sequences to circumvent the

problems associated with preexisting immunity is based on the observation that neutralizing antibodies to common human adeonvirus serotypes are unlikely to cross-neutralize nonhuman viruses. However, the incompatibility of viral and cellular factors imposes a practical limitation on the vast majority of alternative vector systems (bovine, ovine, canine) which are characterized by the disadvantage of having to be propagated in non-human cell lines.

Wilson *et al.* have published a report describing the characterization of a replication-defective vector based on chimpanzee adenovirus type 68 (CV68) C68, which was originally isolated from a mesenteric lymph node of a chimpanzee (Basnight, M., *et. al.* (1971) *Am. J. Epidemiol.* 94:166-171.),CV68 was fully sequenced and found to be similar in overall structure to human adenoviruses (Farina, S. F. *et al., J. Virol.* 75(23): 11603-11613 (2001). The genome of the virus is 36,521 base pairs in length and has been described as being most similar to subgroup E of human adenoviruses, with 90% identity to most human Ad4 open reading frames that have been sequenced. The CV68 ITRs are 130 base pairs in length, and all of the major adenoviral early and late genes are present. CV68 is characterized by a serotype that does not circulate in humans and which lacks neutralizing B cell epitopes that cross-react with those of common human serotypes. Although Chimpanzee adeonviruses are similar to human adenoviruses crossreactive neutralizing immunity against chimpanzee serotypes has not been documented in humans (Farina, S. F. *et al.* J. Virol. (2001) 75(23):11603-13).

The recombinant vectors derived from CV68 are described as being sufficiently similar to human serotypes to support transduction of cells expressing the coxasckievirus and adenovirus receptor (Cohen, C. *et al., J. Gen. Virol.* 83: 151-155 (2002). Significantly, CV68 is characterized by a sufficient level of similarity to human adenoviruses to support its replication 293 cells which harbor E1 from human adenovirus type 5 (Farina, S. F. *et al., J. Virol.* 75(23): 11603-11613 (2001). Furthermore, based on the observation that the flanking sequences of the human serotype 5 E1 are nonhomologous with those of the CV68-derived vector sequences, it is predicted that homologous recombination will not occur. Thus, it has been predicted that there is a low likelihood that CV68-derived vaccine stocks will be contaminated with RCA.

The same group of investigators subsequently reported the use of CV68-derived adenoviral sequences as a vaccine carrier for induction of antibodies to the rabies virus glycoprotein in mice. A replication-defective version of CV68 was created by replacing the E1A and E1B genes with a minigene cassette. Mice immunized with an E1-deletion-containing adenoviral recombinant (AdC68rab.gp) comprising a transgene product encoding the rabies virus glycoprotein developed protective immunity to rabies virus and remained resistant to challenge with an otherwise lethal dose of rabies virus (Xiang, Z *et al., J. Virol.* 76(5): 2667-2675 (2002). A second CV68 construct expressing a codon-optimized, truncated form of gag of

HIV-1 was recently reported to induce a vigorous gag-specific $CD8^+$ T cell response in mice. The vaccine-induced response was shown to provide protection to challenge with a vaccinia gag recombinant virus (Fitzgerald, J. C. *et al., J. Immunol.* 170: 1416-1422 (2003). Experimental vaccination of mice preimmunized to human adenovirus serotype 5 with CV68gag or Ad5gag vectors demonstrated a more pronounced reduction of gag-specific T cells and protection against viral challenge elicited by Ad5 than by CV68 vaccine. The reduction in efficacy of C68gag vaccine was attributed to a cross-reactivity of Ad5-specific CD8+ T cells (*Id.*).

Considered together this data suggests that simian-derived replication-defective adenoviral vectors may be more suitable for use as human vaccine carriers than vectors based on common human serotypes. As shown herein, the results of experiments in which mice that were strongly immunized against human Ad5 (Figure 36) can be immunized with ChAd3-gag adenoviral vectors indicate the preexisiting anti-human Ad5 immunity did not reduce the gag-specific CMI response elicited by the ChAd vectors. These results are consistent with the conclusion that human Ad5 cross-reactive B and T-cell epitopes are not present in ChAd3- or ChAd6 vectors.

Generally speaking, the adenoviral genome is very well characterized and despite the existence of several distinct serotypes, there is some general conservation in the overall organization of the adenoviral genome with specific functions being similarly positioned. The nucleotide sequences of the chimpanzee adenoviruses C1 and CV68 disclosed by Wilson *et al.*, and the location of the E1A, E1B, E2A, E2B, E3, E4, L1, L2, L3, L4 and L5 genes of each virus are provided in U.S. Patent No. 6,083,716 (Chimpanzee Adenovirus Vectors), and PCT published application WO 03/000851 (Methods for Rapid Screening of Bacterial Transformants and Novel Simion Adenoviral Proteins), the teachings of which are incorporated herein by reference.

Each extremity of the adenoviral genome comprises a sequence known as an inverted terminal repeat (ITRs), which is necessary for viral replication. The virus also comprises a virus-encoded protease, which is necessary for processing some of the structural proteins required to produce infectious virions. The structure of the adenoviral genome is described on the basis of the order in which the viral genes are expressed following host cell transduction. More specifically, the viral genes are referred to as early (E) or late (L) genes according to whether transcription occurs prior to or after onset of DNA replication. In the early phase of transduction, the E1, E2, E3 and E4 genes of adenovirus are expressed to prepare the host cell for viral replication. The virus can be rendered replication defective by deletion of the essential early-region 1(El) of the viral genome. Brody *et al*, 1994 *Ann N Y Acad Sci.*, 716:90-101. During the late phase, expression of the late genes L1-L5, which encode the structural

components of the virus particles is switched on. All of the late genes are under the control of a single promoter and encode proteins including the penton (L2), the hexon (L3), the 100 kDa scaffolding protein (L4), and the fiber protein (L5), which form the new virus particle into which the adenoviral DNA becomes encapsidated. Depending on the serotype of the virus, 10,000-100,000 progeny adenovirus particles can be generated in a single host cell. Ultimately, the adenoviral replication process causes lysis of the cells.

The replication-defective adenoviral vectors disclosed herein were constructed by deletion of specific nucleotide sequences from the disclosed chimpanzee nucleic acid sequences and insertion of sequences derived other DNA sequences that are useful for transgene insertion, expression or other genetic manipulations. Accordingly, the recombinant chimpanzee adenoviruses described herein may contain adenoviral sequences derived from one or more chimpanzee adenoviruses, or sequences from a chimpanzee adenovirus and from a human adenovirus. Suitable polynucleotide sequences can be produced recombinantly, synthetically or isolated from natural sources. Adenoviral sequences suitable for use in particular aspects of the invention include sequences which lack neutralizing B-cell epitopes that are cross-reactive with common human serotypes.

At a minimum, the recombinant chimpanzee adenovirus (e.g., vector) of the invention contain the chimpanzee adenovirus *cis*-acting elements necessary for replication and virion encapsidation, in combination with at least one immunogen expression cassette. Typically, the *cis*-acting elements flank the expression cassette which comprises a transgene that encodes at least one antigen. More specifically, the vectors of the invention contain the requisite *cis*-acting 5' inverted terminal repeat (ITR) sequences of the adenoviruses (which function as origins of replication), 3' ITR sequences, packaging/enhancer domains, and a nucleotide sequence encoding a heterologous molecule. Regardless of whether the recombinant vector comprises only the minimal adenoviral sequences or an entire adenoviral genome with only functional deletions in particular genes (e.g., the E1 and/or E3 or E4 regions), the vectors of the invention comprise a chimpanzee adenovirus capsid.

Generally, speaking the adenoviral vectors disclosed herein comprise a replication-defective adenoviral genome, wherein the adenoviral genome does not have a functional E1 gene, and an immunogen expression cassette which comprises: a) a nucleic acid encoding at least one immunogen against which an immune response is desired; and b) a heterologous (i.e., with respect to the adenoviral sequence) promoter operatively linked to the nucleic acid sequence encoding the immunogen(s); and a transcription terminator.

More specifically, the invention provides replication-defective vectors that consist of a recombinant adenoviral genome that is devoid of at least one early gene selected from the

group consisting of E1, E2, E3, and E4. In one embodiment, a replication-defective vector is prepared by replacing, or disrupting, the E1 gene of one of the adenoviral isolates disclosed herein (e.g., ChAd3, ChAd6, ChAd4, ChAd5, ChAd7, ChAd9, ChAd10, ChAd11, ChAd16, ChAd17, ChAd19 or ChAd20) with an immunogen expression cassette. For example, a vector can be prepared by deleting/disrupting the E1 gene of ChAd 3 (SEQ ID NO:1) or ChA6 (SEQ ID NOS: 2). Alternatively, a replication-defective vector can be prepared from any one of the other adenovirus isolates disclosed herein, including ChAd3, ChAd6, ChAd4, ChAd5, ChAd7, ChAd9, ChAd10, ChAd11, Chad16, Chad17, ChAd19 or ChAd20. In other embodiments, replication-defective vectors of the invention comprises an adenoviral genome derived from one of the ChAds disclosed herein that has been optionally engineered to lack a functional E3 gene. It is to be understood that the chimpanzee adenoviral sequences disclosed herein can be rendered replication-defective by either completely removing an early gene or by rendering the gene inoperative or nonfunctional.

It is to be understood that the invention encompasses vectors that are characterized as having modifications, such as a "functional deletion" which destroys the ability of the adenovirus to express one or more selected gene products. The phrase "functional deletion" as used herein broadly encompasses modifications that have the effect of rendering a particular gene product nonfunctional. Generally speaking, functional deletions take the form of a partial or total deletion of an adenoviral gene. However, one of skill in the art will readily acknowledge that other manipulations, including but not limited to making a modification which introduces a frame shift mutation, will also achieve a functional deletion. For example, the recombinant chimpanzee adeonviral vectors of the invention can be rendered replication-defective by introducing a modification that is designed to interfere with, or to functionally delete, the ability of the virus to express adenoviral E1A and/or E1B.

It is well-known that replication-defective adenoviral vectors can be obtained by introducing a modification that is designed to interfere with, or to functionally delete the expression of one o more genes from the group of E2 genes. More in detail, a replication-defective vector can be constructed by inactivating the polymerase gene, or the pre-terminal protein gene or the DNA binding protein gene. Moreover deletion or inactivation of genes expressed by E4 region is an alternative strategy to construct replication-defective chimp Ad vectors. Early gene deletion or inactivation can be combined in order to produce more attenuated vectors. Alternatively, replication-defective ChAd vectors can also comprise additional modifications in other viral genes, such as the late genes L1 through L5. In addition, novel adenoviral vaccine carriers can be generated by combining hexon and fiber genes obtained from different serotypes. The utilization of a hexon and fiber gene shuffling strategy will also allow an

investigator to change the biological properties of a ChAd and facilitate the production of vectors with a different tropism or with new serological characteristics.

It is to be understood that the present invention encompasses recombinant adenoviral vectors comprising deletions of entire genes or portions thereof which effectively destroy the biolgical activity of the modified gene either alone or in any combination. For example, recombinant simian adenoviruses can be constructed which have a functional deletion of the genes expressed by E4 region, although as shown herein it may be desirable to introduce the heterologous Ad5 E4 sequence into the vector in combination with the functional deletion of an E1 gene. Alternatively, the function of the adenoviral delayed early E3 gene may be eliminated; however because the function of E3 is not necessary for the production of a recombinant adenoviral particle it is not necessary to replace this gene product in order to produce a recombinant that is capable of packaging a virus useful in the invention.

In one embodiment of this invention, the replication- defective adenoviral vector used is a chimpanzee subgroup C adenovirus containing deletions in E1 and optionally in E3. For example, for ChAd3, a suitable E1 deletion/disruption can be introduced in the region from bp 460 to bp 3542 (with reference to SEQ ID NO: 1). For ChAd6, a suitable E1 deletion/disruption can be introduced in the region from bp 457 to bp 3425 (with reference to SEQ ID NO: 2). For CV32, the E1 deletion is preferably from bp 456 to bp 3416 (with reference to SEQ ID NO: 3); for CV33, the E1 deletion is preferably from bp 456 to bp 3425 (with reference to SEQ ID NO: 4) and for CV23, the E1 deletion is preferably from bp 456 to bp 3415 (with reference to SEQ ID NO: 5). E3 deletions for CV32 and CV33 are preferably from bp 27446 to bp 31911 (with reference to SEQ ID NO: 3); from bp 27146 to bp 31609 (with reference to SEQ ID NO: 4) respectively. Those of skill in the art can easily determine the equivalent sequences for other chimpanzee isolates based on sequence homologies and multiple sequence alignments.

One of skill in the art will readily acknowledge that in order to construct an E1-deleted adenoviral vector a number of decisions must be made regarding the structure of the vector backbone and the composition of the nucleic acid sequence comprising the transgene. For example, an investigator must determine if the size of the E1 deletion will accommodate the size of the transgene. If not, then additional deletions will have to be introduced into the backbone of the vector.

The nucleic acid sequence embodying the transgene can be a gene, or a functional part of a gene and will typically exist in the form of an expression cassette. Typically a gene expression cassette includes: (a) nucleic acid encoding a protein or antigen of interest; (b) a heterologous promoter operatively linked to the nucleic acid encoding the protein; and (c) a

transcription termination signal. The nucleic acid can be DNA and/or RNA, can be double or single stranded. The nucleic acid can be codon-optimized for expression in the desired host (*e.g.*, a mammalian host).

Decisions must also be made regarding the site within the backbone where the transgene will be introduced and the orientation of the transgene. More specifically, the transgene can be inserted in an E1 parallel (transcribed 5' to 3') or anti-parallel (transcribed in a 3' to 5' direction relative to the vector backbone) orientation. In addition, appropriate transcriptional regulatory elements that are capable of directing expression of the transgene in the mammalian host cells that the vector is being prepared for use as a vaccine carrier in need to be identified and operatively linked to the transgene. "Operatively linked" sequences include both expression control sequences that are contiguous with the nucleic acid sequences that they regulate and regulatory sequences that act in *trans*, or at a distance to control the regulated nucleic acid sequence.

Regulatory sequences include: appropriate expression control sequences, such as transcription inititation, termination, enhancer and promoter sequences; efficient RNA processing signals, such as splicing and polyadenylation signals; sequences that enhance translation efficiency (e.g., Kozak consensus sequences); sequences that enhance protein stability, and optionally sequences that promote protein secretion. Selection of these and other common vector elements are conventional and many suitable sequences are well known to those of skill in the art (see, e.g., Sambrook *et al*, and references cited therein at, for example, pages 3.18-3.26 and 16.17-16.27 and Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons, New York, 1989).

In specific embodiments, the promoter is a heterologous promoter (i.e., with respect to the adenovirus sequences) which is recognized by an eukaryotic RNA polymerase. In a preferred embodiment, the promoter is a "strong" or "efficient" promoter. An example of a strong promoter is the immediate early human cytomegalovirus promoter (Chapman *et al*, 1991 *Nucl. Acids Res* 19:3979-3986, which is incorporated by reference). The human CMV promoter can be used without (CMV) or with the intron A sequence (CMV-intA), although those skilled in the art will recognize that any of a number of other known promoters, such as the strong immunoglobulin, or other eukaryotic gene promoters may be used, including the EF1 alpha promoter, the murine CMV promoter, Rous sarcoma virus (RSV) promoter, SV40 early/late promoters and the beta-actin promoter.

Further examples of promoters that can be used in the present invention are the strong immunoglobulin promoter, the EF1 alpha promoter, the murine CMV promoter, the Rous Sarcoma Virus promoter, the SV40 early/late promoters and the beta actin promoter, albeit those

of skill in the art can appreciate that any promoter capable of effecting expression in the intended host can be used in accordance with the methods of the present invention. The promoter may comprise a regulatable sequence such as the Tet operator sequence. Sequences such as these that offer the potential for regulation of transcription and expression are useful in instances where repression of gene transcription is sought.

Suitable gene expression cassettes will also comprise a transcription termination sequence. A preferred transcriptional terminator is the bovine growth hormone terminator. The promoter/transcription termination combination of CMVintA-BGH terminator is particularly preferred although other promoter/terminator combinations may also be used. As shown herein, the bovine growth hormone termination/polyadenylation signal (bGHpA) or short synthetic polyA signal (SPA) of 50 nucleotides in length defined as follows: AATAAAAGATCTTTATTTTCATTAGATCTGTGTGTT-GGTTTTTTGTGTG (SEQ ID NO:26). Generally speaking, exemplify suitable termination sequences. The polyA signal is inserted following the nucleic acid sequence which comprises the transgene and before the 3' adenovirus ITR sequence.

The recombinant adenoviral vectors described herein may contain adenoviral sequences derived from one or more strain of adeonvirus. Suitable sequences may be obtained from natural sources, produced recombinantly, synthetically, or by other genetic engineering or chemical methods. In a particular embodiment, the recombinant chimpanzee adenovirus is a chimeric recombinant comprising non-chimpanzee adenoviral polynucleotide sequences. Suitable non-chimpanzee adenoviral sequences can be obtained from human adenoviral strains. For example, the native E4 region can be replaced by hAd5 E4 (Ad5 nt 32816 to nt 35619) or by Ad5E4orf6 (Ad5 nt 33193 to nt 34077) (Ad5 GenBank Accession No: M73260).

Generally speaking, the immunogen (antigenic molecule) delivered by the recombinant adenoviral vector of the invention comprises a polypeptide, protein, or enzyme product which is encoded by a transgene in combination with a nucleotide sequence which provides the necessary regulatory sequences to direct transcription and/or translation of the encoded product in a host cell. The composition of the transgene depends upon the intended use of the vector. For example, if the immunogenic composition is being designed to elicit an antibody response or a cell-mediated immune response in a mammalian host which is specific for an infectious agent, then it is appropriate to utilize a nucleic acid sequence encoding at least one immunogenic product that is predicted to confer pathogen-specific immunity to the recipient. Alternatively, if the composition is being prepared for use as a cancer vaccine, a suitable transgene may comprise an immunogenic portion of a self-antigen, such as a TAA, which has been selected with the goal of eliciting a protective immune response of sufficient potency to

both break host tolerance to a particular TAA and to elicit a long-lived (e.g., memory) response that will be sufficient to prevent the initiation of cancer or to prevent tumor progression. Accordingly, suitable immunogenic gene products may be obtained from a wide variety of pathogenic agents (such as, but not limited to viruses, parasites, bacteria and fungi) that infect mammalian hosts, or from a cancer or tumor cell. Although, the invention is illustrated herein with a particular set of test immunogens it is to be understood that the invention is not limited to the use of the antigens exemplified herein. More specifically, the invention contemplates the use of both heterologous and self-antigens as immunogens, including but not limited to TAAs.

In one embodiment, the invention provides an immunogenic composition (e.g., a vaccine) for inducing an immune response against antigens (i.e., immunogens) expressed by an infectious agent. For example, it is desirable to elicit an immune response against a virus infecting humans and/or non-human animal species. Examples of virus families against which a prophylactic and/or therapeutic immune response would be desirable include the *Picornaviridae* family which includes six different genera such as Aphtovirus, Cardiovirus, Enterovirus, Hepatovirus, Parechovirus, Rhinovirus. Examples of Picornavirus against which an immuneresponse would be desirable are: Foot-and-mouth disease viruses, Encephalomyocarditis viruses, Polioviruses, Coxackieviruses, Human hepatitis A virus, Human parechoviruses, Rhinoviruses. *Caliciviridae* family includes different genera associated with epidemic gastroenteritis in humans caused by the Norwalk group of viruses and other syndromes in animals like the hemorrhagic disease in rabbits associated with rabbit hemorrhagic disease virus or respiratory disease in cats caused by feline calicivirus.

Another family of viruses, against which it may be desirable to elicit an immune response is the *Astroviridae* which comprises viruses isolated from humans as well as many different animal species. Human astroviruses are associated with gastroenteritis and young children diarrhea. Alternatively, it may be desirable to confer mammalian hosts with immunity to members of the *Togaviridae* family of viruses which comprises two genera: alphavirus and rubivirus. Alphaviruses are associated with human and veterinary diseases such as arthritis (i.e. Chikungunya virus, Sindbis virus) or encephalitis (i.e. Eastern Equine Encephalitis Virus, Western Equine Encephalitis Virus).

Rubella virus provides an alternative viral target against which is the only member of the Rubivirus genus is responsible for outbreaks of a mild exanthematic disease associated with fever and lymphoadenopathy. Rubella virus infection is also associated with fetus abnormalities when acquired by mother during in early pregnancy. *Flaviviridae* is an other virus family consisting of three genera: the flaviviruses, the pestiviruses and the hepaciviruses that includes important human as well as animal pathogens. Many of the flavivirus genus members

are arthropod-borne human pathogens causing a variety of diseases including fever, encephalitis and hemorrhagic fevers. Dengue Fever Viruses, Yellow Fever Virus, Japanese Encephalitis Virus, Wst Nile Fever Virus, Tick-borne Encephalitis Virus are pathogens of major global concern or of regional (endemic) concern. Pestivirus genus includes animal pathogens of major economic importance such as Bovine Viral Diarrhea Virus, Classical Swine Fever Virus, Border Disease Virus. Hepatitis C Virus is the only member of the Hepacivirus genus responsible for acute and chronic hepatitis. HCV proteins expressed by a recombinant adenovirus can elicit a protective as well as therapeutic immune response limiting the consequences of a viral infection affecting 170 million people worldwide.

Alternatively, antigens derived from members of the *Coronaviridae* family can be expressed by recombinant adenovirus vectors in order to obtain protection against infection. Protection against the severe acute respiratory syndrome coronavirus (SARS-Co Virus) can be obtained by immunizing with one or more chimpanzee adenovirus choosen from the group including ChAd3, 4, 5,6, 7,9,10,11,16,17,19, 20 expressing one or more SARS-CoV protein including without limitations nucleocapsid (N) protein, polymerase (P) protein, membrane (M) glycoprotein, spike (S) glycoprotein, small envelope (E) protein or any other polypeptide expressed by the virus. *Rhabdoviridae* family members including rabies virus can be target of recombinant vaccine expressing viral proteins.

Other possible targets include the *Filoviridae* family comprising Ebola-like viruses and Marburg-like viruses genera, that is responsible of outbreaks of severe hemorrhagic fever; the *Paramyxoviridae* family comprising some of the most prevalent virus known in humans like measles, respiratory syncytial, parainfluenza viruses and viruses of veterinary interest like Newcastle disease and rinderpest viruses; the *Orthomyxoviridae* family including Influenza A,B,C viruses; *Bunyaviridae* family mainly transmitted by arthropod to vertebrate hosts comprising important human pathogens like Rift valley fever, Sin Nombre , Hantaan, Puumala viruses; *Arenaviridae* family comprising Lymphocytic choriomeningitis, Lassa fever, Argentine Hemorragic fever, bolivian Hemorragic fever viruses; *Bornaviridae* family comprising viruses causing central nervous system diseases mainly in horses and sheep;*Reoviridae* family including rotaviruses , the most important cause of severe diarrheal illness in infants and young children worldwide, orbiviruses that can affect both humans and other mammals (bluetongue, epizootic hemorrhagic disease viruses); Retroviridae family, a large group of viruses comprising important human pathogens like human immunodeficiency virus 1 and 2 (HIV-1 and HIV-2) and human t-cell leukemia virus type 1 and 2 (HTLV 1 and 2) as well as non-human lentivirus such as Maedi/Visna viruses affecting sheep and goats, Equine infectious anemia virus affecting horses, bovine immunodeficiency virus affecting cattle, feline immunodeficiency virus affecting

cats; Polyomaviridae family groups small DNA oncogenic viruses, prototype viruses are polyoma and SV40 infecting mouse and rhesus monkey respectively, (BK and JC viruses closely related to SV40 were isolated from human patients); *Papillomaviridae* family consists of a group of DNA viruses infecting higher vertebrates including humans generating warts and condylomas. Papilloma viral infection is associated with the development of cancer in both humans and animals. Human papilloma viruses are associated with cervical cancer, vaginal cancer and skin cancer. The herpesviridae famils includes subfamilies in which are classified a number of important pathogens for humans and other mammals. Suitable sources of antigens can be but are not limited to herpes simplex viruses 1 and 2, varicella-zoster virus, Epstein-Barr virus, Cytomegalovirus, human herpesviruses 6A,6B and 7, Kaposi's sarcoma-associated herpesvirus. Further suitable source of antigens are members of the Poxviridae family like Monkeypox virus, Molluscum contagiusum virus, smallpox virus; Hepatitis B virus, the prototype member of the hepadnaviridae family as well as other virus causing acute and/or chronic hepatitis like hepatitis delta virus, hepatitis E virus.

The adenoviral vectors of the present invention are also suitable for the preparation of immunogenic compositions designed to stimulate an immune response in humans or animals against protein expressed by non-viral pathogens including bacteria, fungi, parasites pathogens For example,the vectors disclosed herein can be used to prepare vaccines against, but not limited to: *Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae, Vibrio cholerae, Clostridium tetani, Neisseria meningitis, Corynebacterium diphteriae, Mycobacteria tuberculosis and leprae, Listeria monocytogenes,* and *Legionella pneumofila.* Examples of fungi and mammalian parasites for which it may be desirable to prepare prophylactic or therapeutic vaccines include: *Candida albicans, Aspergillus fumigatus, Histoplasma capsulatum, Plasmodium malariae, Leishmania major, Trypanosome cruzi and brucei, Schistosoma haematobium , mansoni and japonicum; Entamoeba histolytica,* and numerous species of Filaria known to be responsible for human filariasis.

Cancer typically involves the deregulation of genes that encode polypeptides which contribute to maintaining cell cycle or controlling cell proliferation (e.g., growth factors, oncogenes, receptors and tumor suppressors). The products of many of the genes implicated in cancer are expressed on the surface of a wide variety of tumor cells. A variety of tumor antigens that may be recognized by T and B lymphocytes have been identified in human and animal cancer. The vast majority of human tumor-associated antigens (TAAs) that are suitable for use in an anticancer vaccine trial are described as "self-antigens" due to the fact that in addition to being expressed on tumor cells they also are expressed on normal tissue and/or during fetal

development. Immunotolerance of the target population to TAAs may explain why many cancer vaccines have proven to be ineffective.

Tumor antigens can be produced by oncogenic mutants of normal cellular genes altered proto-oncogenes or tumor suppressor genes such as Ras, p53 or Bcr-Abl protein are examples of altered cellular proteins that can stimulate T/B cell response. Tumor antigens can be normal cellular proteins that are overexpresses in tumor cells (tyrosinase, GP100, MART are normally expressed at low levels in melanocytes and overexpressed in melanoma) or aberrantly expressed in tumor cells (MAGE, BAGE, GAGE expressed in melanomas and many carcinomas but normally expressed in the testis and placenta). Tumor antigens can be products of oncogenic viruses: papillomavirus E6 and E7 proteins expressed by cervical carcinomas; EBV EBNA-1 protein produced by EBV+ lymphomas and nasopharyngeal carcinomas; SV40 T antigen in SV40 induced experimental tumors. Oncofetal antigens are expressed to high levels on cancer cells and in normal developing (fetal) tissues but not in adult tissues. Carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP) are examples of well characterized oncofetal antigens.

Recent evidence supports the existence of TAAs that are capable of eliciting an immune response, thus making this class of antigens suitable immunogens for vaccine therapy. However, as a class of antigens TAAs are notoriously poor immunogens and T cells that are highly specific for TAAs are either deleted or anergized during T-cell development. Accordingly, there is an expectation that the immune response of a tumor-bearing host to a particular TAA will be extremely weak. Because of the inherent need to break host tolerance to a target TAA experimental clinical vaccine studies are particularly focused on developing immunization strategies that will enhance TAA-specific T-cell responses. Generally, speaking an effective cancer vaccine must both overcome immunotolerance and enhance host's immune response to a level that is preventitive and/or protective. Anti-tumor effects in many experimental vaccine studies have been correlated with T-cell responses to TAAs.

In an alternative embodiment, the invention contemplates an immunogenic composition (e.g., a cancer vaccine) which can be used to induce an immune response against tumor antigens. A suitable composition would contain a recombinant chimpanzee adenovirus comprising nucleic acid sequence encoding a tumor antigen and a physiologically acceptable carrier. In a particular embodiment, the coding sequence element of the cassette may encode a single immunogen, such as an immunogenic peptide sequence derived from a self-antigen, such as a tumor-associated antigen. In some embodiments, the nucleic acid sequence encoding the immunogen (i.e., the transgene) may be codon optimized for expression in a particular mammalian species. In other embodiments, the coding sequence may encode more than one immunogen, such as one or more codon optimized tumor antigens. For example, a cancer

vaccine utilizing the disclosed adenoviral vectors may encode a combination of self-antigens such as: HER2/neu, CEA, Hepcam, PSA, PSMA, Telomerase, gp100, Melan-A/MART-1, Muc-1, NY-ESO-1, Survivin, Stromelysin 3, Tyrosinase, MAGE3, CML68, CML66, OY-TES-1, SSX-2, SART-1, SART-2, SART-3, NY-CO-58, NY-BR-62, hKLP2, VEGF.

Development of an effective cancer vaccine requires the identification of a strategy that will elicit antigen-specific immunity in vaccinated patients and the generation of an immune response that will persist after active immunization has ended. The success of the strategy will depend on whether a measurable immune response directed against a target antigen will correlate with protection against cancer occurrence or relapse. The effector mechanisms of both cell-mediated immunity and humoral immunity have been show to kill tumor cells. However, data from experimental systems suggest that antigen-specific T cells represent the most powerful immunologic mechanism for the elimination of tumor cells. Recognition of tumor-specific antigens (e.g., TAAs) by effector T-cells is predicted to allow the TAA to function as a tumor-rejection antigen. Published studies suggest that stimulation of $CD8^+$ and $CD4^+$ helper T-cell responses are important for achieving optimal tumor clearance ((Greenberg, P. D. (1991) *Adv. Immunol.* 49: 281-355; Pardoll, D. M. *et al.* (1998) *Curr. Opin. Immunol.* 10: 588-94). Clinical response (i.e., efficacy) has been associated with increases in interferon γ-secreting cytotoxic T cells. The advent of assays, such as the ELISPOT assay used herein, to demonstrate the efficacy of the instant vaccine carriers, allows investigators to measure T-cell responses to vaccination regimens and thereby facilitates the development of cancer vaccines.

Cancer vaccines can be either prophylactic or therapeutic. The general assumption underlying the prophylactic use of cancer vaccines is that TAAs are extremely weak immunogens or functionally nonimmunogenic in tumor-bearing subjects. More specifically, in the field of cancer immunology, vaccines can be used as immunotherapy in patients afflicted with cancer. Accordingly, cancer vaccines can be designed to elicit an immune response that is that is directed against a TAA that is expressed by a pre-existing tumor or malignancy. Thus, in particular embodiments, therapeutic cancer vaccines are intended for use in tumor-bearing patients who have developed resistance to conventional regimens of treatment or who have a high probability of developing a recurrence following conventional treatment.

The high immunogenicity of adenoviruses, make adenoviral vectors particularly good candidates for use in the context of a vaccine carrier designed to break host tolerance to a self-antigen. The phenomenon of epitope or determinant spreading, which was first described in autoimmune diseases, has been associated with both MHC class I- and MHC class II-restricted responses and correlated to the development of HER-2/neu protein-specific T-cell immunity. Epitope spreading represents the generation of an immune response to a particular portion of an

immunogenic protein followed by the natural spread of immunity to other antigenic determinants present on the same protein. For example, Disis *et al.* observed epitope spreading in 84% of patients afflicted with HER-2/neu overexpressing malignancies who were administered vaccines comprising peptides derived from potential T-helper epitopes of the HER-2 protein mixed with granulocyte-macrophage colony stimulating factor (*J. Clin. Oncol.* (2002) 20(11): 2624-2632). Importantly, epitope spreading was correlated with the generation of a HER-2/neu protein domain response and suggests that immunization effectively circumvented immunologic tolerance.

TAAs that are suitable for use in the disclosed adenoviral vectors and methods as a target for a cancer vaccine should possess a number of characteristics. For example, a target TAA must have a favorable expression profile, meaning that it should be preferentially expressed or overexpressed in the tumor or malignant tissue as compared with normal tissue. In addition, because TAAs that play a role in tumorigenesis are more likely to be retained during the different stages of cancer progression, a suitable target TAA should also preserved throughout tumor progression and metastases. Suitable target TAAs should also be expressed homogenously within the tumor. Third, suitable target TAAs must not be subject to absolute immunologic tolerance. More specifically, there should be some evidence that T cells which can both recognize and respond to the TAA of interest have not been entirely deleted from the host's T-cell repertoire (Berinstein, N. L., *J. Clin. Oncol.* 29(8): 2197 (2002).

Carcinoembryonic antigen (CEA) has many characteristics which make it an attractive TAA for use as a target antigen for an anticancer vaccine. It is a member of the Ig superfamily which is characterized by a favorable expression pattern. It is expressed in more than 50% of all human cancers and has been implicated in the tumorigenesis process, which suggests that its expression may be selected and conserved throughout cancer progression. In addition, it has been established that immunologic tolerance to CEA is not absolute. Published studies establish that human T cells can recognize, become activated to, and lyse cancer cells that express CEA (Berinstein, N. L., J. *Clin. Oncol.* 29(8): 2197 (2002). For example, the immunization of patients with recombinant vaccinia virus expressing CEA, combined with subsequent peptide-based in vitro stimulations, generated CD8+ MHC-restricted CTLs capable of lysing autologous tumors (Tsang, K. Y. *et al. J. Natl. Cancer Inst.*, (1995) 87:982-990). Alternatively, immunization of colorectal carcinoma patients after surgery with recombinant CEA was reported to induce weak antibody and cellular responses to recombinant CEA (Samanci, A., *et al.* (1998) *Cancer Immunol. Immunother.* 47: 131-142.) Further, the administration of anti-CEA anti-idiotypic antibody to patients diagnosed with colorectal cancer generated anti-CEA antibodies and idiotype-specific T-cell proliferation (Foon, L, A. *et al.*

(1995) *J. Clin. Invest..*, 96: 334-342). The literature also indicates that tolerance to CEA in cancer patients can be overcome with several different vaccination approaches (i.e., vaccination with recombinant CEA or recombinant orthopox or avipox-CEA viruses, administration of anti-idiotype antibodies, pulsing dendritic cells with CEA agonist epitopes).

CEA is an oncofetal glycoprotein that is expressed in normal fetal colon and to a much lesser extent in normal colonic mucosa. It is also overexpressed in the vast majority of adenocarcinomas, particularly those of the colon, pancreas, breast, lung, rectum and stomach. Many colorectal cancers and some carcinomas produce high levels of CEA that are measurable in sera, which makes it one of the most widely used serological markers of malignancy, especially in patients with colorectal cancer.

A second TAA which provides a suitable immunogen for use in the compositions and methods of the invention is product of the HER2/erb-2 (also called neu) proto-oncogene. Like, CEA, HER2/neu has a favorable expression pattern and is not subject to absolute tolerance. More specifically, low levels of expression of the HER2/neu transcript, and the 185 kD polypeptide product, are detected in normal adult epithelial cells of various tissues, including the skin and breast, and tissues of the gastrointestinal, reproductive, and urinary tracts; higher levels of expression are detected in the corresponding fetal tissues during embryonic development (Press *et al.*, *Oncogene* 5: 953-962 (1990). Several lines of evidence suggest a link between the amplification of HER-2 and neoplastic transformation in human breast, lung, prostate, ovarian, endometrial and colorectal tumors (Disis and Cheever, *Adv. Cancer Research 71*: 343-371(1997). Generally speaking, overexpression of HER2/neu correlates with a poor prognosis and a higher relapse rate for cancer patients (Slamon *et al.*, *Science* 244: 707-712 (1989). Thus, a vaccine specific for the HER-2/neu protein could have wide application and utility in the prevention of disease recurrence in many different human malignancies.

HER2/neu encodes a transmembrane glycoprotein possessing intrinsic tyrosine kinase activity and displaying extensive homology to the epidermal growth factor (EGF) receptor (Akiyama, T *et al.*, (1986) Science 232: 1644-1646). One of the first clinical studies which utilized HER2 as target for cancer immunotherapy employed the HER-2-specific monoclonal antibody Herceptin for the treatment of breast cancer (Goldenberg MM (1999) Clin. Ther. 21: 309-318). This led to subsequent efforts which focused on the use of HER-2 as a target for the T-cell arm of the immune system to elicit effective antitumor responses, including the use of recombinant fusion proteins comprising HER-2 domains to activate autologous antigen presenting cells. Published reports establish that numerous cancer patients afflicted with neu-expressing mammary and ovarian cancers mount immune responses (e.g., produce antigen-specific antibody and T-cells) against the protein product of the HER2/neu oncogene.

Assembly of the recombinant adenoviral sequences, transgene and other vector elements into various intermediate plasmids and shuttle vectors, and the use of the plasmids and vectors to produce a recombinant viral particle are all achieved using conventional techniques as described in standard textbooks that are well known to those of skill in the art (Sambrook *et al*, Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Press, Cold Spring Harbor, NY (1989). Such techniques include, but are not limited to conventional cDNA cloning techniques, use of overlapping oligonucleotde sequences derived from the adenoviral genome, homologous recombination, polymerase chain reaction, standard transfection techniques, plaquing of viruses in agar overlay and other related methodologies.

To assist in preparation of polynucleotides in prokaryotic cells, a plasmid version of the adenovirus vector is often prepared (adenovirus pre-plasmid). The adenovirus pre-plasmid contains an adenoviral portion and a plasmid portion. The adenoviral portion is essentially the same as the adenoviral portion contained in the adenoviral vectors of the invention (containing adenoviral sequences with non-functional or deleted E1 and optionally E3 regions) and an immunogen expression cassette, flanked by convenient restriction sites.

The plasmid portion of the adenovirus pre-plasmid often contains an antibiotic resistance marker under transcriptional control of a prokaryotic promoter so that expression of the antibiotic does not occur in eukaryotic cells. Ampicillin resistance genes, neomycin resistance genes and other pharmaceutically acceptable antibiotic resistance markers may be used. To aid in the high level production of the polynucleotide by fermentation in prokaryotic organisms, it is advantageous for the adenovirus pre-plasmid to contain a prokaryotic origin of replication and be of high copy number. A number of commercially available prokaryotic cloning vectors provide these benefits. It is desirable to remove non-essential DNA sequences. It is also desirable that the vectors not be able to replicate in eukaryotic cells. This minimizes the risk of integration of polynucleotide vaccine sequences into the recipients' genome. Tissue-specific promoters or enhancers may be used whenever it is desirable to limit expression of the polynucleotide to a particular tissue type.

Adenovirus pre-plasmids (plasmids comprising the genome of the replication-defective adenovirus with desired deletions and insertions) can be generated by homologous recombination using adenovirus backbones DNA and an appropriate shuttle vector (designed to target-in specific deletions and incorporate desired restriction sites into the resultant plasmid). Shuttle vectors of use in this process can be generated using general methods widely understood and appreciated in the art, *e.g.*, PCR of the adenoviral terminal ends taking into account the desired deletions, and the sequential cloning of the respective segments into an appropriate cloning plasmid. The adenoviral pre-plasmid can then be digested and transfected into the

complementing cell line via calcium phosphate co-precipitation or other suitable means. Virus replication and amplification then occurs, a phenomenon made evident by notable cytopathic effect. Infected cells and media are then harvested after viral replication is complete (generally, 7-10 days post-transfection).

Generally speaking, following the construction and assembly of the desired adenovirus pre-plasmids, adenovirus pre-plasmids are rescued into virus by transfecting an adenoviral E1-expressing human cell line. Complementation between the packaging cell line and the viral genes of the vector permits the adenovirus-transgene sequences in the vector to be replicated and packaged into virion capsids, resulting in the production of recombinant adenoviruses. The resulting viruses may be isolated and purified by any of a variety of methods known to those of skill in the art for use in the methods of the invention.

It will be readily apparent to those of skill in the art that when one or more selected deletions of chimpanzee adenoviral genes are introduced into a viral vector, the function of the deleted gene product can be supplied during the production process by sequences present in the production cell line. Thus, the function of the manipulated genes can be provided by a permanently transformed cell line that is characterized by some or all of the adenoviral functions which are required for packaging but which are not functional in the vector (e.g., any of E1A, E1B, E2A, E2B E4). Alternatively, the requisite adenoviral functions can be provided to a suitable packaging cell line by infecting or transiently transfecting a suitable cell with a construct comprising the requisite gene to provide the function.

Accordingly, the present invention also provides a method of producing chimpanzee adenoviral vectors in E1-expressing human cell lines. More specifically, the disclosed vectors can be propagated in an E1 complementing cell lines, including the known cell lines 293 and PER.C6™. Both these cell lines express the adenoviral E1 gene product. PER.C6™ is described in WO 97/00326, published January 3, 1997, which is hereby incorporated by reference. It is a primary human retinoblast cell line transduced with an E1 gene segment that complements the production of replication deficient first generation adenoviruses, but is designed to prevent generation of replication competent adenovirus by homologous recombination. 293 cells are described in Graham *et al* (1977) *J. Gen. Virol* 36:59-72, which is also hereby incorporated by reference. One of skill in the art will recognize the term "first generation adenovirus" refers to a replication deficient adenovirus which has either a non-functional or deleted E1 region, and optionally a non-functional or deleted E3 region.

Batches of replication-defective adenoviral vectors that are intended for use as a vaccine composition in a clinical trial should be proven to be free of RCA (Fallaux, F.J. *et al* (1998) *Humm Gene Therapy*, 9:1909-1917). In practice, this is a labor intensive process which

requires establishing and utilizing an expensive screening program. One of skill in the art will acknowledge that a high frequency of RCA generation not only results in a high failure rate for the batches produced, but also severely limits scale-up efforts. Elimination of sequence homology between the nucleotide sequence of the vector and the adenoviral sequences present in the genome of the helper production/packaging cell line should eliminate the possibility of producing batches of vector that are contaminated with RCAs produced by homologous recombination.

Typically, recombinant replication-defective adenoviral vectors are propagated in cell lines that provide E1 gene products *in trans*. Supplementation of the essential E1 gene products *in* trans is very effective when the vectors are from the same or a very similar serotype. For example, it is well-known that E1-deleted (i.e. ΔE1) group C serotype (Ad2 and Ad5) vectors, can be propagated in 293 or PER.C6 cells which contain and express the Ad5 E1 region. However, it has been observed that Ad5 E1 sequences present in the 293 and PER.C6 production cells may not always fully complement the replication of non-group C serotypes. Accordingly, E1-deleted serotypes outside of subgroup C, for example those from subgroups A, B, D, E, and F may replicate with a lower efficiency respect to the corresponding wt virus or may not replicate at all in 293 or PER.C6 cells. This may be due to the inability of the Ad5 (group C) E1B 55K gene product to establish a functional interaction with the E4 orf6 gene product of the non-group C serotypes.

The decrease in replication efficiency in cells expressing Ad5 E1 is variable considering vectors of different subgroups. While ΔE1 vectors deriving from subgroup D and E adenovirus can be rescued and propagated in 293 and Per.C6™ cells with variable efficiency, the propagation ΔE1 vectors of subgroup B is completely impaired (Vogels R, *et. al.* (2003) Aug. Replication-deficient human adenovirus type 35 vectors for gene transfer and vaccination: efficient human cell infection and bypass of preexisting adenovirus immunity. *J Virol.*; 77 (15):8263-71).

Although the interaction between Ad5 E1b 55k and vector-expressing E4 orf6 protein is conserved within members of the same subgroup, it may be not sufficiently stable when E4 orf6 protein of a non-C serotype is expressed. This inefficient or unstable formation of E1B-55K/E4-orf6 complex lead to an absent of reduced propagation of the ΔE1 vector. Accordingly, it has been empirically determined that in order to successfully and efficiently rescue recombinant adenovirus of groupB serotypes, a cell line expressing the E1 region of the serotype of interest may need to be generated. In cells expressing Ad5E1 like 293 or Per.C6™, the expression can be limited to E1b 55K protein. Alternatively, a suitable Ad5E1-expressing cell lines could be modified to express the entire Ad5 E4 region (or E4 orf6 only) in addition to

Ad5E1. The generation of cell lines expressing both Ad5 E1 and orf6 are useful in complementing alternative adenovirus serotypes; *see, e.g.,* Abrahamsen *et al.*, 1997 *J. Virol.* 8946-8951. The incorporation of E4 (orf6) into Ad5 complementing cell lines, is known, as is the generation of serotype-specific cell lines providing a serotype-specific E1 gene product(s) *in trans.* Alternatively, the efficiency of non-group C vector propagation may be improved by modification of the viral backbone by substituting the native E4 region with Ad5 orf6. Similar results can be achieved by substituting the only the native orf6 with orf6 deriving from Ad5 or other subgroup C viruses (Ad1, Ad2, Ad6).U.S. Patent No. 5,849,561 discloses complementation of an E1-deleted non-group C adenovirus vector in an Ad5-E1 complementing cell line which also expresses portions of the Ad5-E4 gene.

U.S. Patent No. 6,127,175, issued to Vigne, *et al.*, discloses a stably transfected mammalian cell line which expresses a portion of the E4 region of adenovirus, preferably orf6/orf6/7. Such a cell line is useful for complementation of recombinant Ad genomes deficient in the E4 region.

Compositions, including vaccine compositions, comprising the disclosed adenoviral vectors are an important aspect of the present invention. These compositions can be administered to mammalian hosts, preferably human hosts, in either a prophylactic or therapeutic setting. Potential hosts/vaccinees include but are not limited to primates and especially humans and non-human primates, and include any non-human mammal of commercial or domestic veterinary importance. Compositions comprising recombinant chimpanzee adenoviral vectors may be administered alone or in combination with other viral- or non-viral-based DNA/protein vaccines. They also may be administered as part of a broader treatment regimen.

In a particular embodiment of the invention, the disclosed vectors may be used in an immunization protocol designed to break host tolerance to a self-antigen or a tumor-associated antigen. The identification of a number of TAA has enabled the development of active vaccination approaches for the therapy of cancer. Both cell surface antigens and intracellular antigens that are processed and presented provide useful targets. Generally speaking, the disclosed method of breaking host tolerance to a self-antigen comprises: (a) stimulating an antigen-specific response to a self-antigen by administering a first vaccine composition comprising a first ChAd vector or a plasmid vector carrying a nucleotide sequence encoding the self-antigen against which an antigen-specific immune response is desired, and (b) sustaining and expanding the immune response of (a) by administering a second vaccine composition comprising a recombinant ChAd vector of a different serotype containing at least a functional deletion of its genomic E1 gene, and in the site of the E1 gene, a sequence comprising a promoter capable of directing the expression of DNA encoding the same self-antigen delivered in the

priming step, whereby the host mounts an immune response which has the effect of breaking tolerance to the self-antigen.

Accordingly, a skilled artisan can utilize this disclosure to design several different immunization protocols that may be suitable for use to break host tolerance. For example, it may be possible to utilize a protocol in which the first, or priming immunization comprises plasmid DNA which encodes a particular self-antigen, such as a TAA, and any subsequent immunizations comprise a ChAd vector. Plasmid DNA sequences comprising nucleotide sequences that encode self-antigens, may be delivered intramuscularly, with or without electrostimulation, in one or more injections. For example, an immunization protocol based on multiple (e.g., 3 or 4 or 5) intramuscular injections of plasmid DNA encoding a TAA via electroporation followed by one or more intramuscular injections of a ChAd vector comprising a transgene encoding the same TAA is encompassed by the general method disclosed and claimed herein.

Alternatively, a suitable protocol to break tolerance could involve one or more priming immunizations with a ChAd or hAd vector comprising a transgene encoding a self antigen, followed by one or more boosting immunizations with either the same, or a different ChAd vector that is know to be non cross-reactive with the vector used for the priming immunization(s). For example, an immunization protocol using ChAd3 for priming and ChAd6 for boosting, or ChAd3 for priming followed by ChAd6 and ChAd9 for boosting could be used to break host tolerance. In particular embodiments, the invention contemplates the use of self-antigens comprising at least one tumor associated antigen selected from the group consisting of: HER2/neu, CEA, EpCAM, PSA, PSMA, Telomerase, gp100, Melan-A/MART-1, Muc-1, NY-ESO-1, Survivin, Stromelysin 3, Tyrosinase, MAGE3, CML68, CML66, OY-TES-1, SSX-2, SART-1, SART-2, SART-3, NY-CO-58, NY-BR-62, hKLP2, VEGF. In a particular embodiment, the invention provides a method for inducing an immune response (e.g., humoral or cell-mediated) to a tumor-associated antigen which is specific for a selected malignancy by delivering a recombinant chimpanzee adenovirus encoding the TAA to a mammal afflicted with cancer. In a preferred embodiment of this aspect of the invention the elicited immune response constitutes an immune response characterized by the production of antigen-specific CD4+ and CD8+ T cells.

The immunogenic compositions of the invention can be administered to mammalian hosts, preferably human hosts, in either a prophylactic or therapeutic setting. Potential hosts/vaccinees include but are not limited to primates and especially humans and non-human primates, and include any non-human mammal of commercial or domestic veterinary importance. Compositions comprising recombinant chimpanzee adenoviral vectors may be

administered alone or in combination with other viral- or non-viral-based DNA/protein vaccines. They also may be administered as part of a broader treatment regimen. Suitable compositions, for use in the methods of the invention may comprise the recombinant viral vectors of the invention in combination with physiologically acceptable components, such as buffer, normal saline or phosphate buffered saline, sucrose, other salts and polysorbate. It does not cause tissue irritation upon intramuscular injection. It is preferably frozen until use. Optionally, a vaccine composition of the invention may be formulated to contain other components, such as but not limited to, an adjuvant, a stabilizer, a pH adjusting agent, or a preservative. Such components are well known to those of skill in the art.

It is envisioned that the recombinant chimpanzee adenoviruses of the invention will be administered to human or veterinary hosts in an "effective amount," that is an amount of recombinant virus which is effective in a chosen route of administration to transduce host cells and provide sufficient levels of expression of the transgene to invoke an immune response which confers a therapeutic benefit or protective immunity to the recipient/vaccine.

The amount of viral particles in the vaccine composition to be introduced into a vaccine recipient will depend on the strength of the transcriptional and translational promoters used and on the immunogenicity of the expressed gene product. In general, an immunologically or prophylactically effective dose of $1x10^7$ to $1x10^{12}$ particles (i.e., $1x10^7$, $2x10^7$, $3x10^7$, $5x10^7$,$1x10^8$, $2x10^8$, $3x10^8$, $5x10^8$ or $1x10^9$, $2x10^9$, $3x10^9$, $5x10^9$) and preferably about $1x10^{10}$ to $1x10^{11}$ particles is administered directly into muscle tissue. Subcutaneous injection, intradermal introduction, impression through the skin, and other modes of administration such as intraperitoneal, intravenous, or inhalation delivery are also contemplated.

The recombinant chimpanzee adenoviral vectors of the present invention may be administered alone, as part of a mixed modality prime/boost vaccination regimen or in a vaccination regimen based on combination of multiple injections of different vector serotypes. Typically, a priming dose(s) comprising at least one immunogen is administered to a mammalian host in need of an effective immune response to a particular pathogen or self-antigen. This dose effectively primes the immune response so that, upon subsequent identification of the antigen(s), the host is capable of immediately mounting an enhanced or boosted immune response to the immunogen. A mixed modality vaccination scheme which utilized alternative formulations for the priming and boosting can result in an enhanced immune response. Prime-boost administrations typically involve priming the subject (by viral vector, plasmid, protein, *etc.*) at least one time, allowing a predetermined length of time to pass, and then boosting (by viral vector, plasmid, protein, *etc.*). Multiple immunizations, typically 1-4, are usually employed, although more may be used. The length of time between priming and boost

may typically vary from about four months to a year, albeit other time frames may be used as one of ordinary skill in the art will appreciate. Multiple injection of each vector can be administered within approximately a 2 weeks time frame, before neutralizing immunity becomes evident.

In some embodiments of this invention, a vaccine is given more than one administration of adenovirus vaccine vector, and it may be given in a regiment accompanied by the administration of a plasmid vaccine. Suitable plasmid vaccines for use in combination with the vectors disclosed herein comprise a plasmid encoding at least one immunogen against which a primed or boosted immune response is desired, in combination with a heterologous promoter, which is capable of directing expression of the nucleic acid sequences encoding the immunogen(s), operably linked to the immunogen coding sequence, and a transcription terminator sequence.

For example, a dosing regimen which utilizes multiple injection of different serotypes of recombinant replication-defective chimpanzee adenoviral vectors can be used. Alternatively, an individual may be given a first dose (i.e., a priming dose) of a plasmid vaccine, and a second dose (i.e., a boosting dose) which comprises a replication-defective recombinant chimpanzee adenoviral vector which comprises a coding sequence for the same immunogen that was delivered in the plasmid vaccine. Alternatively, the individual may be given a first dose of a human adenovirus vaccine vector encoding at least one immunogen, followed by a second dose comprising a replication-defective recombinant chimpanzee adenoviral vector disclosed herein, which comprises a coding sequence for the same immunogen that was delivered in the priming dose. In a second alternative embodiment a vaccine composition comprising a vector of the invention may be administered first, followed by the administration of a plasmid vaccine. In any of these embodiments, an individual may be given multiple doses of the same immunogen in either viral vector or plasmid form. There may be a predetermined minimum amount of time separating the administrations.

In addition to a single protein or antigen of interest being delivered by the recombinant, replication-defective chimpanzee adenovirus vectors of the present invention, two or more proteins or antigens can be delivered either via separate vehicles or delivered *via* the same vehicle. Multiple genes/functional equivalents may be ligated into a proper shuttle plasmid for generation of a adenovirus pre-plasmid comprising multiple open reading frames. Open reading frames for the multiple genes/functional equivalents can be operatively linked to distinct promoters and transcription termination sequences.

As shown herein, suitable immunization regimens can employ different adenoviral serotypes. One example of such a protocol would be a priming dose(s) comprising a recombinant adenoviral vector of a first serotype, for example a ChAd3 or ChAd6 followed by a

boosting dose comprising a recombinant chimpanzee adenoviral vector of a second serotype. In an alternative embodiment, the priming dose can comprise a mixture of separate adenoviral vehicles each comprising a gene encoding for a different protein/antigen. In such a case, the boosting dose would also comprise a mixture of vectors each comprising a gene encoding a separate protein/antigen, provided that the boosting dose(s) administers recombinant viral vectors comprising genetic material encoding for the same or similar set of antigens that were delivered in the priming dose(s). These multiple gene/vector administration modalities can further be combined. It is further within the scope of the present invention to embark on combined modality regimes which include multiple but distinct components from a specific antigen.

Use of recombinant vectors derived from chimpanzee adenoviruses that are not neutralized by preexisting immunity directed against the viral elements of human vector offers an alternative to the use of human Ad vectors as vaccine carriers. Because adenoviruses are highly immunogenicity, adenoviral vectors are particularly good candidates for use in the context of a vaccine carrier designed to break host tolerance to a self-antigen. Furthermore, the ability to propagate the chimp viruses in human cells, particularly in the Per.C6™™ cell line, with an efficiency comparable to human viruses, offers considerable advantages both from a regulatory point of view and for the large scale production of therapeutics or vaccines. Accordingly, the instant invention provides a collection of chimpanzee adenoviral sequences, vectors and plasmids that allow the preparation of recombinant virus which may be used, alone or in combination, as a vaccine carrier for genetic vaccination.

All publications mentioned herein are incorporated by reference for the purpose of describing and disclosing methodologies and materials that might be used in connection with the present invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

Having described preferred embodiments of the invention with reference to the accompanying drawings, it is to be understood that the invention is not limited to those precise embodiments, and that various changes and modifications may be effected therein by one skilled in the art without departing from the scope or spirit of the invention as defined in the appended claims.

The following examples illustrate, but do not limit the invention.

EXAMPLE 1 ISOLATION, CLONING, SEQUENCING AND CHARACTERIZATION OF ChAds

Chimpanzee Adenovirus Isolation

Stool specimens were collected in viral transport medium (VTM; Microtest M4-R Multi-Microbe Transport Medium, Remel Inc.) then frozen or frozen directly at –70°C at NIRC (New Iberia Research Center 4401 W. Admiral Doyle Drive New Iberia, LA 70560). The specimens were kept frozen at < -70°C until they were processed for inoculation into cell cultures. At that time, the specimens were thawed and then vortexed in excess of chilled viral transport medium. After the specimens had dissociated into suspensions, they were centrifuged for 10 min at 1500-1800 rpm. The supernatants were filtered through 0.8 and 0.2 μm syringe filters in series and then the filtered material was inoculated into cell cultures (200-250 μL into shell vials and 250-300 μL into tube cultures). Each processed specimen was inoculated into tube cultures and shell vial cultures seeded with 293 cells or A549 cells.

Control (positive and negative) cultures were prepared each time a set of samples was inoculated. Once all of the shell vials in a set-up had been inoculated, they were centrifuged at room temperature for 60 ± 10 min at 2000 rpm (900 x g). The vials were removed from the centrifuge immediately after the rotor stopped spinning to prevent heat damage in the cultures. After centrifugation, the inocula were aspirated from the shell vials, using a fresh sterile pasteur pipet in each vial to prevent cross-contamination. The cultures were washed three times using 1.0-mL fresh culture medium for each wash. Fresh medium (1.0 mL) was pipetted into each vial after the third wash and the shell vials were placed in an incubator at 35-37°C for three to four days (approx. 96 hr).

At the end of the culture period, the supernatants were aspirated from the cultures and the cell layer in each vial was washed twice with Immunofluorescence Assay (IFA) Buffer using approximately 1.0 mL buffer with each wash. The cells were fixed by adding 1.0 mL refrigerated acetone to each vial (10 min at 2-8°C. Acetone-cleaned slides were labeled with the specimen identification number(s) associated with the shell vial coverslips. The shell vial coverslips were processed for fluorescence labeling of Adenovirus-infected cells using a primary mouse anti-adenovirus antibody [MAB8052, Chemicon]. The slides are evaluated with the aid of a fluorescence microscope. Each preparation was scanned using the 10X objective noting the extent of immunofluorescence coverage across the well (1+ to 4+). The presence or absence of specific immunofluorescence was confirmed using the 40X objective. Tube cultures were inoculated in the same sequence as described for the shell vials (e.g., negative control first, followed by clinical specimens and positive controls). The inocula were allowed to adsorb for

60-120 min at 36-38°C. After the adsorption period, the specimens/controls were aspirated from the tubes and replaced by fresh culture medium.

Three to four days post-inoculation, and once a week thereafter, the media was aspirated from the culture tubes and replaced with 1.5 mL fresh media. Culture tubes were visually monitored for CPE at least every other day for at least 21 days after inoculation. Cultures inoculated with chimp specimens were compared against the controls and rated by observing the CPE extent. Cultures showing no CPE were passed to fresh tube cultures after 14 days; culture tubes that were negative for CPE after 21 days were considered negative. Culture tubes with 3-4+ CPE were vortexed for 10 seconds. The cells were scraped from the wall of the tube using a sterile 1.0 mL serological pipet and suspended in the culture supernatant. After labeling a 5 mL snap cap tube with the specimen identification number and date and stored at –70°C. 500 µL of the cell suspension was transferred from the culture tube into the snap cap tube and stored for up to one day at 2-8°C until it was processed using an indirect immunofluorescent antibody technique to detect adenovirus (equivalent to procedure for staining shell vials).

Chimpanzee Adenovirus Amplification

Wild type chimp adenoviruses CV32, CV33, CV23 and CV68 purchased from the ATCC (ATCC Accession Numbers: CV32, VR-592; CV-33, VR-593;) or from Esoterix Inc. Austin, Texas and original isolates were propagated as follows by using the human E1-expressing cell line PER.C6™ or 293. Briefly, cells were cultivated in Dulbecco's Modified Eagles Medium (DMEM; GibcoBRL, Life Technologies) supplemented with 10% Fetal Bovine Serum (FBS GibcoBRL, Life Technologies), 1% Penicillin-Streptomycin, 2mM Glutamine and 10mM $MgCl_2$ (Per.C6™). Adenovirus infection was carried out in DMEM supplemented with 5% Horse Serum (GibcoBRL, Life Technologies). Infected cells and medium were collected when 100% of the cells exhibited virus-induced cytopathic effect (CPE) and lysed by three cycles of freezing and thawing.

All wild type chimp adenoviral (CV) stocks were cloned by infecting 293 cells seeded in 96-well plates, after the first passage of amplification. The virus cloning was performed by limiting dilution of the cell lysate obtained at the first passage of the virus amplification. 5 isolated clones were picked up and serially propagated. After 3-4 serial passaging of amplification, a large-scale preparation of adenovirus was performed on cells planted on 5 two-layer cell-factories (NUNC) (200 millions of cells/cell factory). Purified viral particles were obtained from cell lysate by two ultra-centrifugation steps on cesium chloride density gradients.

Sequencing of Viral Genomic DNA

Genomic DNA was isolated from 3 X 10^{12} pp of purified virus preparation by digestion with Proteinase K (0.5 mg/ml) in 1% SDS-TEN (2 hrs at 55°C). After a Phenol-Chloroform extraction and Ethanol precipitation, the genomic DNA was resuspended in water and submitted for genomic sequencing.

For full length Ad genome sequencing, the purified viral DNA was nebulized to produce randomly sheared fragments. The DNA fragments were blunt-ended with the klenow fragment of E.coli DNA polymerase and polynucleotide kinase. The blunt end fragment were run on a low melting point agarose gel to purify the fragments in the size range of 1-3 kb and cloned into the SmaI site of pUC19 vector to create a shotgun library. The ligations were used to transform competent XL1-Blue MRF'. Positive colonies were identified by white/blue screening on LB agar containing X-gal and IPTG. Three to four 96-well block of plasmid DNA were isolated from the library and sequenced with pUC forward and reverse primers. All sequencing reads were screened for quality and vector sequence using the Phred-Phrap software package. The reads that passed the screening were assembled into contigs. Primers were designed to directly sequence the adenoviral DNA for closing the gaps and determine the DNA sequence of both ends.

Complete viral genome sequencing was obtained for selected viruses including ChAd3 (SEQ ID NO: 1), ChAd6 (SEQ ID NO: 2) and CV32 (SEQ ID NO:3), CV33 (SEQ ID NO: 4), and CV23 (SEQ ID NO:5). Table 1 provides data summarizing the percentage of identity between the nucleotide sequences of ChAd3, ChAd6, Pan5 (CV23), Pan6 (CV32), Pan7 (CV33), C1 and C68 adenoviral genomes. Alignments were calculated using the ALIGN program as part of the FASTA package version 2 (William R. Penson, University of Virginia; Myers & Miller, CABIOS 1989, 4:11-17).

Table 1. Percentage of Nucleotide Sequence Identity Between Chimpanzee Adenovirus Genomes

	ChAd3	ChAd6	Pan5	Pan6	Pan7	C1	C68
ChAd3	100	68.1	68.5	68.2	68.3	64.2	68.0
ChAd6		100	95.5	94.5	95.5	73.6	91.4
Pan5			100	94.9	96.7	73.9	92.7
Pan6				100	95.1	73.6	91.3
Pan7					100	73.8	93.0
C1						100	74.3
C68							100

To characterize the new adenoviral isolates (e.g., ChAd20, ChAd4, ChAd5, ChAd7, ChAd9, ChAd10, ChAd11, ChAd16, ChAd17 and ChAd19) the nucleotide sequence of the hexon and fiber genes were also determined by primer walking. Fiber gene: SEQ ID NOS: 6-15: (SEQ ID NO: 6, ChAd20); SEQ ID NO: 7, ChAd4); SEQ ID NO: 8, ChAd5); SEQ ID NO: 9, ChAd7); SEQ ID NO: 10, ChAd9); SEQ ID NO: 11, ChAd10); SEQ ID NO: 12, ChAd11); SEQ ID NO: 13, ChAd16) SEQ ID NO: 14, ChAd17) and SEQ ID NO: 15, ChAd19). Figures 20A-20D provide a comparison of the amino acid sequences of the fiber proteins of the ChAd isolates disclosed and claimed herein.

The hexon gene sequences are set forth in SEQ ID NOS: 16-25: (SEQ ID NO: 16, ChAd20); SEQ ID NO: 17, ChAd4); SEQ ID NO: 18, ChAd5); SEQ ID NO: 19, ChAd7); SEQ ID NO: 20, ChAd9); SEQ ID NO: 21, ChAd10); SEQ ID NO: 22, ChAd11); SEQ ID NO: 23, ChAd16); SEQ ID NO: 24, ChAd17) and SEQ ID NO: 25, ChAd19). Figures 31A-31M provide a comparison of the amino acid sequences of the hexon proteins of the ChAd isolates disclosed and claimed herein.

Chimpanzee Adenovirus Classification

Classification of the different chimp adenoviral strains follows the already proposed classification of human adenovirus serotypes into 6 subgroups (Horowitz, MS (1990) Adenoviridae and their replication. In Virology B.N. Fields and D.M. Knipe, eds (Raven Press, New York) pp.1679-1740) and it was obtained by amino acid and nucleotide sequence alignment by using Align X program (Informax, Inc).

An initial classification of the new isolates was obtained by looking at the restriction pattern of the viral genome with different restriction endonucleases and by sequence

analysis of the hypervariable region 7 (HVR7) of the hexon gene. To this end two primers were designed on the highly conserved regions flanking HVR7: TGTCCTACCARCTCTTGCTTGA (SEQ ID NO.45) and GTGGAARGGCACGTAGCG (SEQ ID NO.46). The HVR7 was amplified by PCR using purified viral DNA or crude 293 lysate as template and then sequenced. Based on HVR7 sequence analysis we classified the new isolated viruses into the subgroups (A-F) proposed for human Ad viruses (Horowitz, MS (1990) Adenoviridae and their replication. In Virology B.N. Fields and D.M. Knipe, eds (raven Press, New York) pp.1679-1740).

The phylogenetic tree presented in Figure 35 was obtained by alignment of human and chimp adenovirus hexon amino acid sequences. The results are consistent with the initial classification based on nucleotide sequence alignment limited to hexon HVR7 by using Align X program (Informax, Inc). The tree was deduced from a multiple sequence alignment of full-length hexon peptide sequences using a PAUPSEARCH (Wisconsin Package Version 10.3, Accelrys Inc.) and visualized and manipulated with TREEVIEW. Bootstrap confidence analysis was performed using the PAUPSEARCH program as implemented in the Wisconsin Package. For each of the alignments the program was run on 1000 replicates using "Heuristic Search" as search criterion and Maximum Parsimony as the optimality criterion and confidence values reported were taken from a 50% majority-rule consensus.

EXAMPLE 2 ChAd SHUTTLE VECTOR AND EXPRESSION VECTOR CONSTRUCTION AND RESCUE

Vector Construction and Rescue

Genomic viral DNA was cloned into a standard plasmid vector by homologous recombination with an appropriate shuttle vector containing viral DNA sequences derived from both left and right end of viral genome (Figure 2). As described more fully below, the sequence homology observed between viruses classified in the same serotype subgroup was exploited to develop group-specific shuttle vectors. Genomic viral DNA of Chimp adenovirus classified into subgroup D and E resulted to be sufficiently homologous to allow the construction of a common shuttle vector in order to clone viruses belonging to both subgroups.

Construction of a Subgroup D/E Shuttle Vector

The ChAd6 viral genome was fully sequenced (SEQ ID NO: 2) and the information obtained was used to construct a shuttle vector to facilitate cloning by homologous recombination of subgroup D and E chimpanzee adenovirus.

Construction of the ChAd6 shuttle vector, referred to herein as

pARS ChAd6-3 is described in Figure 1. Figure 32 provides a list of the oligonucleotide sequences (SEQ ID NOS: 26-40 and SEQ ID NOS: 45-46) used in the cloning experiments described herein. Briefly, 457 bp deriving from the left end of ChAd6 DNA were amplified by PCR with the oligonucleotides 5'-ATGGAA
TTCGTTTAAACCATCATCAATAATATACCTC-3 (SEQ ID NO: 27) and
5'- CGCTGGCACTCAAGAGTGGCCTC-3' (SEQ ID NO: 28) digested with EcoRI and SnaBI and cloned into pNEBAd35-2 cut EcoRI-SnaBI, generating pNEBChAd6-LI. The right ChAd6 ITR (bp 36222 to bp 36648) was amplified by PCR using the oligonucleotides:
5'- ATGAAGCTTGTTTAAACCCAT CATCAATAATATACCT-3 '
(SEQ ID NO: 29) and 5'- ATCTAGACAGCGTCCATAGCTTACCG-3'
(SEQ ID NO: 30) digested with restriction enzymes HindIII and XbaI and cloned into pNEBChAd6-LI HindIII-XbaI digested thus generating pNEBChAd6-RLI. Finally, the DNA fragment corresponding to nucleotides 3426-3813 of the ChAd6 genomic DNA sequence was amplified with the olinucleotides:
5' ATGCTACGTAGCGATCGCGTGAGTAGTGTTTGGGGGTGGGTGGG-3' (SEQ ID NO: 31) and
5'- TAGGCGCGCCGCTTCTCCTCGTTCAGGCTGGCG-3' (SEQ ID NO: 32), digested with SnaBI and AscI then ligated with SnaBI-AscI digested pNEBChAd6-RLI thus generating pNEBChAd6-RLIdE1.

To improve the efficiency of recombination and plasmid propagation in DH5a *E.coli* strain, the 1306 bp fragment containing both left and right ITRs of ChAd6 as well as pIX gene fragment was excised by PmeI digestion from pNEBChAd6-RLIdE1 and transferred to a different plasmid vector obtained by PCR amplification with the olinucleotides 5'-
GATCTAGTTAGTTTAAACGAATTCGGATCTGC
GACGCG-3' (SEQ ID NO: 33) and 5' TTCGATCATGTTTAAACGAA
ATTAAGAATTCGGATCC-3' (SEQ ID NO: 34) from pMRKAd5SEAP. This final ligation step generated the ChAd6 shuttle vector pARSChAd6-3.

Construction of a Subgroup C Shuttle Vector

The ChAd3 viral genome was fully sequenced (SEQ ID NO: 1) and the information obtained was used to construct a shuttle vector to facilitate cloning by homologous recombination of subgroup C chimpanzee adenovirus.

Briefly, the shuttle vector used to clone subgroup C chimp adenovirus, referred to herein as pChAd3EGFP was constructed as follows: a ChAd3 DNA fragment (nt 3542-4105) containing pIX coding region was amplified by PCR with the oligonucleotides 5'-

TATTCTGCGATCGCTGAGGTGGGTGAGTGGGCG-3' (SEQ ID NO: 35) and 5'-TAGGCGCGCCCTTAAACGGCATTTGTGGGAG-3' (SEQ ID NO: 36) digested with SgfI-AscI then cloned into pARSCV32-3 digested with SgfI- AscI, generating pARS-ChAd3D. ChAd3 right end (nt 37320-37441) was amplified by PCR with oligonucleotides 5'-CGTCTAGAAGACCCGAGTCTTACCAGT-3' (SEQ ID NO: 37) and 5'-CGGGATCCGTTTAAACCATCATCAATAATATACCTTATT-3' (SEQ ID NO: 38) digested with XbaI and BamHI then ligated to pARS-ChAd3D restricted with XbaI and BamHI, generating pARS-ChAd3RD. ChAd3 viral DNA left end (nt 1-460) was amplified by PCR with oligonucleotides 5'- ATGGAATTCGTTTAAACCATCATCAATAATATACCTT-3' (SEQ ID NO: 39) and 5'- ATGACGCGATCGCTGATATCCTATAATAATAAAACGCAGACTTTG-3', (SEQ ID NO: 40) digested with EcoRI and SgfI then cloned pARS-ChAd3RD digested with EcoRI and SgfI, thus generating pARS-ChAd3RLD. The viral DNA cassette was also designed to contain restriction enzyme sites (PmeI) located at the end of both ITR's so that digestion will release viral DNA from plasmid DNA.

Construction of ΔE1 Chimp Adenoviral Vectors

Subgroup C: Subgroup C chimp adenovirus vectors were constructed by homologous recombination in *E.coli* strain BJ5183. BJ5183 cells were co-transformed with pChAd3EGFP shuttle vector digested with BstEII and Bst1107I and ChAd3, ChAd11, ChAd19 and ChAd20 purified viral DNA. . Homologous recombination between pIX genes ,right ITR DNA sequences present at the ends of linearized pChAd3EGFP and viral genomic DNA allowed its insertion in the plasmid vector, deleting at the same time the E1 region that was substituted by EGFP expression cassette. Expression cassettes based on human cytomegalovirus (HCMV) promoter and bovine growth hormone polyadenylation signal (Bgh polyA) were constructed to express secreted alkaline phosphatase (SEAP), EGFP, HIV gag , HCV NS region (as described in fig.3 for ChAd6 shuttle vectors) as well as tumor-associated antigens like CEA and HER2/neu from human and Rhesus monkey origin.

Subgroups D and E: In order to construct ΔE1 vectors based on subgroup D and E chimp adenovirus, the shuttle vector pARS ChAd6-3 was digested with AscI and co-transformed into *E.coli* strain BJ5183 with CV32, CV33, CV68, ChAd4, ChAd5, ChAd6, ChAd7, ChAd9, ChAd10 and ChAd16 purified viral DNA. Homologous recombination between DNA sequences from pIX genes and right ITR present at the ends of linearized pARS ChAd6-3 and viral genomic DNA allowed its insertion in the plasmid vector, deleting at the same time the E1 region (figures 2 and 4).

Expression cassettes based on human cytomegalovirus (HCMV) promoter and bovine growth hormone poly-adenylation signal (Bgh polyA) were constructed to express secreted alkaline phosphatase (SEAP), EGFP, HIV gag , HCV NS genes (Figure 3) as well as tumor-associated antigens like CEA and HER2/neu of human and Rhesus monkey origin. All the expression cassette were inserted into the single SnaBI site of pARS ChAd6-3 vector to be transferred by homologous recombination into the ΔE1 adenovirus pre-plasmids as described in figure 4.

Rescue and amplification of ΔE1 Vectors

$5X10^6$ PER.C6™ cells planted on 6cm cell culture dishes were transfected with 10 micrograms of cloned viral vector released from plasmid sequences by endonuclease digestion. DNA transfection was performed using Lipofectamine (Invitrogen). Transfected cells and culture medium were collected 5-10 days post-transfection and lysed by freeze-thaw. Rescued vectors were then amplified by serial passaging on 293 or PER.C6™ cells. A large-scale amplification was performed by infecting cells planted on 5-10 cell-factories (NUNC, Inc.) on a total of $1\text{-}2x10^9$ cells. A purified vector preparation was obtained on cesium chloride gradient by two ultra-centrifuge runs, dialyzed against PBS containing 10% glycerol and stored at –70°C in aliquots.

EXAMPLE 3 NEUTRALIZATION STUDIES

Neutralization assays were carried out in order to evaluate the prevalence in human sera of neutralizing antibodies against the chimpanzee adenoviruses disclosed herein. The assay evaluated the effects of serum preincubation on the ability of chimp adenoviruses carrying the gene for secreted alkaline phosphatase (SEAP) to transduce human 293 cells. The neutralization titer is defined as the dilution of serum giving a 50% reduction of the SEAP activity observed in the positive control with the virus alone.

From $2x10^6$ to $1.5x10^7$ physical particles of CV33-SEAP, CV32-SEAP and ChAd3-SEAP vector were diluted in 100 µl of complete medium and added to an equal volume of human or chimp serum diluted in complete medium. Each serum samples was tested at various dilutions (five 4-fold increments starting from 1/18 dilution through 1:4608). Samples were pre-incubated for one hour at 37°C and then added to 293 cells seeded into 96-well plates ($3x10^4$ cells/well). The inoculum was removed after one hour of incubation, the cells were re-fed with fresh medium and, 24 hours later, 50 µl of medium was removed and the SEAP activity was measured by a chemiluminescent assay. The neutralization titer is defined as the dilution of serum giving a 50% reduction of the SEAP activity observed in the positive control with the virus alone. A panel of 100 human sera was tested for ChAd neutralization activity. In parallel the same panel was tested on Ad5 SEAP vector.

Table 2. Prevalence of neutralizing antibodies against chimpanzee adenovirus

	Virus			
titer	hAd5	CV32	CV33	ChAd3
< 200	77%	96%	100%	92%
> 200	33%	4%	0%	8%

The result provided in Table 2 indicates that a very low prevalence in human sera of neutralizing antibodies directed against vector derived from chimpanzee adenoviruses. Only four sera showed a titer over the threshold of 200 on CV32 vector while 8 showed a titer over 200 on ChAd3 SEAP vector. On the contrary, the panel of chimp sera examined showed a very high prevalence of anti-Chimp Ad immunity. These findings confirm that as expected, vectors based on chimp Ads have a very little chance to be neutralized in humans. Therefore they represents an ideal solution to the problem of the pre-existing anti-human Ad immunity that limits the administration of viral vectors based on common human Ad serotypes such as Ad5.

MURINE IMMUNIZATION STUDIES

METHODS AND MATERIALS

Immunization Protocols and Splenocyte /PBMC Preparation

Immunizations: Mice were immunized with the selected adenoviruses diluted in 0.1 ml of buffer. Each vector dose was divided in two aliquot of 50 µl and injected in both quadriceps of mice.

Splenocyte Preparation: Mice were sacrificed 3 weeks post-injection and their spleens excised and transferred in 10 ml of R10 (10% FCS, 55mM 2-mercaptoethanol, 1M HEPES buffer, 2mM L-glutamine, 1X penicillin-streptomicine solution in RPMI medium 1640). Spleens were minced through a steel screen and, after the screen was washed with 2 ml of R10, splenocytes were transferred in a 50 ml Falcon tube and centrifuged at 1200 rpm, 10 min, room temperature (rt). Supernatant was removed and 3 ml of ACK lysis buffer (Gibco BRL Formulation#79-0422DG) were added. Cells were incubated 5 min, rt. 45 ml of 1X PBS were

added and tubes were centrifuged as above. After washing with 30 ml of R10, cells were resuspended in 5 ml of R10, filtered through a 70 m Nylon cell strainer (Falcon 2350). 10µl of cells were diluted with 990 µl Turk's solution (Merck 040417345) and counted. Cells were finally diluted to 10^7 cells /ml in R10.

Peripheral blood mononuclear cell (PBMC) preparation: Mice blood samples (150 ul) were transferred to 2ml eppendorf tubes with 50ul PBS/2% EDTA. 1 ml ACK buffer was added to each tube. Gently mixed and incubated at RT for 5 min. Samples were centrifuged at 1500rpm in microcentrifuge for 5 min. Supernatant was discharged white cell pellets deriving from the same immunized cohorts were combined. ACK buffer incubation was repeated then pellets of PBMC were resuspended in 1 ml of R10 medium.

IFN-γ ELISPOT Assay

Millipore MAIP 45 plates were coated with 100 µl/well of purified rat anti-mouse IFN-γ monoclonal antibody (Pharmingen, cat. 551216) diluted at 2.5 µg/ml in PBS and incubated over-night (o/n) at 4^0C. Plates were washed 2X with sterile PBS and un-specific binding sites were blocked by incubation for 2hrs in the CO_2 incubator with 200 µl/well of R10. In the immunization experiments with Ad vectors expressing HIV gag, a 9-mer peptide (AMQMLKETI, a CD8 HIV gag epitope mapped in Balb/C mice) (SEQ ID NO: 47) was diluted to 2 µg/ml in R10 and added to the wells in the amount of 50 µl/well. In immunization experiments conducted with HCV-NS expressing vectors, a pool of peptides covering NS3 helicase domain as well a 9-mer peptide representing a mapped CD8 epitope comprised in helicase domain were used. Immunization experiments with ChAds expressing human CEA antigen were evaluated by pools of overlapping 15-mer peptides covering the entire amino acid sequence. As controls DMSO and Concanavalin A were used. Cells were added to each well at the amount of $5X10^5$ and $2.5X10^5$. After an o/n incubation in the CO_2 incubator, plates were washed with 0.05% Tween 20/PBS and 50 µl/ well of biotinylated rat anti-mouse IFN-γ monoclonal antibody (PharMingen cat. 554410) diluted 1/250 in assay buffer (5%FBS, 0.005% Tween20, PBS) were added. Plates were incubated o/n at 4^0C and washed as above. Streptavidin-alkaline phosphatase conjugate (BD554065) was diluted 1 /2500 in assay buffer and added in the amount of 50 µl/well for 2 hrs rt. After washing, plates were developed adding 50

µl/well of BCIP/NBT1-step solution (Pierce 34042). Reaction was stopped by washing wells with deionized water. Spots were automatically counted by an ELISPOT reader.

Murine IFN-γ Intracellular Staining (ICS)

Splenocytes were diluted at $2X10^6$ cells in 1 ml of R10 and stimulated with the same antigens described above at the concentration of 2 µg/ml. As controls, DMSO and Staphylococcal Enterotoxin B (SEB) were used. After an overnight incubation in the CO_2 incubator, cells were washed with FACS buffer (1% FCS, 0.01% NaN3, PBS) and purified anti-mouse CD16/CD32 Fc block (clone 2.4G2, Pharmingen cat. 553142) was diluted 1/25, added in the amount of 100 µl/sample and incubated for 15min at 4^0C. Cells were washed in FACS buffer and APC conjugated anti-mouse CD3e (clone 145-2C11, Pharmingen #553066), PE conjugated anti-mouse CD4 (clone L3T4, BD Pharmingen cat. 553142) and PerCP conjugated anti-mouse CD8a (clone 53-6.7, Pharmingen cat. 553036) diluted 1:50 in FACS buffer were added in the amount of 100 µl/sample. Cells were incubated 30 min rt, washed, fixed and permeabilized (Becton Dickinson, FACS Perm 2) and incubated with FITC conjugated anti-mouse IFN-γ Pharmingen cat.554411) diluted 1:50 in PermWash (100 ul/sample) for 30 min at RT. After washing cells were resuspended in 500 ul 1% formaldehyde/PBS and intracellular cytokine staining (ICS) analyzed on a FACS-Calibur flow cytometer, using CellQuest software (Becton Dickinson).

EXAMPLE 4 ChAd VECTORS ELICIT STRONG CMI RESPONSES IN MICE

The ability of the ChAd vectors disclosed herein to elicit a cell-mediated immune response (CMI) was evaluated in mice using vectors expressing an HIV gag transgene. Briefly, groups of 5 Balb/C mice were injected with ten-fold increasing doses of the different vectors starting from 10^5 up to 10^{10} vp/mouse.

The strength of the immune response was determined three weeks after the injection by quantifying gag-specific CD8+ T cells in the splenocytes. The number of IFN-γ secreting CD8+ T cells was determined by ELISPOT assay or by IFN-γ intracellular staining and FACS analysis after stimulation *in vitro* with a peptide reproducing a gag CD8+ T cell epitope mapped in Balb/C mice.

The results obtained from the 5 immunized animals, reported in Table 3, are expressed as spot forming cells per 10^6 splenocytes. Shown are the number of spot forming cells per million splenocytes following incubation with 9-mer CD8+ gag epitope or with gag peptide pool. The gag peptide pool consisted of 20-aa peptide overlapping by 10aa encompassing the entire gag sequence. Positive values are reported in bold.

The data provided in Table 3 indicate that the administration of the ChAd vectors disclosed and claimed herein elicts a strong cell mediated immune response which is comparable to the response elicited by hAd5. By looking at the lowest vector dose resulting in a positive immunization result (immunization breakpoint), we ranked the potency of the different vectors being subgroup C ChAd3gag the most potent with a breakpoint at 10^6 pp vector dose. Ranking by immunization break-points is shown in Figure 33.

Table 3. **Gag-specific T cell response in BalbC mice immunized with chimpanzee Ad vectors.**

Vaccination	10^5 vp		10^6 vp		10^7 vp		10^8 vp		10^9 vp		10^10 vp	
	mock	Gag	mock	Gag	mock	Gag	mock	Gag	mock	Gag	mock	Gag
ChAd3DE1gag	1	neg	1	944	1	1298	1	1258	NT	NT	NT	NT
	3	neg	1	1039	1	1958	1	1962	NT	NT	NT	NT
	1	neg	1	859	1	1923	1	1931	NT	NT	NT	NT
	1	neg	1	1620	1	1388	1	1389	NT	NT	NT	NT
	1	neg	1	1529	5	1442	4	1436	NT	NT	NT	NT
CV33DE1gag	NT	NT	1	neg	2	475	1	2910	NT	NT	NT	NT
	NT	NT	1	neg	1	433	1	401	NT	NT	NT	NT
	NT	NT	1	neg	1	243	1	634	NT	NT	NT	NT
	NT	NT	1	neg	1	505	2	3457	NT	NT	NT	NT
	NT	NT	1	neg	1	583	2	1684	NT	NT	NT	NT
CV68DE1gag	NT	NT	3	neg	1	340	2	332	0	406	2	635
	NT	NT	1	neg	1	512	0	535	1	256	3	1172
	NT	NT	0	neg	2	458	3	944	2	462	2	505
	NT	NT	7	neg	0	148	1	519	0	488	2	1184
	NT	NT	0	neg	2	1418	1	243	0	240	1	789
ChAd9DE1gag	NT	NT	1	neg	7	369	1	609	NT	NT	NT	NT
	NT	NT	1	neg	1	508	1	739	NT	NT	NT	NT
	NT	NT	1	neg	1	299	16	291	NT	NT	NT	NT
	NT	NT	1	neg	2	507	8	926	NT	NT	NT	NT
	NT	NT	0.5	neg	1	36	40	1034	NT	NT	NT	NT
ChAd10DE1gag	NT	NT	1	neg	1	83	1	822.5	NT	NT	NT	NT
	NT	NT	1	neg	1	42.5	1	1033	NT	NT	NT	NT
	NT	NT	1	neg	1	48	1	1339.5	NT	NT	NT	NT
	NT	NT	1	neg	4	51	1	1132	NT	NT	NT	NT
	NT	NT	1	neg	1	486.5	1	521.5	NT	NT	NT	NT
ChAd6DE1gag	NT	NT	1	neg	1	34	1	721	NT	NT	NT	NT
	NT	NT	1	neg	10	4	1	560	NT	NT	NT	NT
	NT	NT	1	neg	1	24	1	624	NT	NT	NT	NT
	NT	NT	1	neg	1	225	3	3002	NT	NT	NT	NT
	NT	NT	1	neg	1	276	4	1736	NT	NT	NT	NT
ChAd11DE1gag	1	neg	1	neg	0	573	NT	NT	NT	NT	NT	NT
	0	neg	0	neg	0	919	NT	NT	NT	NT	NT	NT
	0	neg	1	neg	1	1438	NT	NT	NT	NT	NT	NT
	2	neg	0	neg	0	0	NT	NT	NT	NT	NT	NT
	1	neg	1	neg	0	456	NT	NT	NT	NT	NT	NT
ChAd20DE1gag	0	neg	0	neg	0	1	NT	NT	NT	NT	NT	NT
	2	neg	0	neg	0	408	NT	NT	NT	NT	NT	NT
	0	neg	0	neg	0	414	NT	NT	NT	NT	NT	NT
	1	neg	0	neg	0	2	NT	NT	NT	NT	NT	NT
	0	neg	0	neg	1	311	NT	NT	NT	NT	NT	NT
ChAd7DE1gag	NT	NT	1	neg	1	neg	1	1044	NT	NT	NT	NT
	NT	NT	3	neg	1	neg	1	606	NT	NT	NT	NT
	NT	NT	1	neg	8	neg	1	407	NT	NT	NT	NT
	NT	NT	1	neg	1	neg	2	567	NT	NT	NT	NT
	NT	NT	1	neg	3	neg	1	1677	NT	NT	NT	NT
CV32DE1gag	NT	NT	NT	NT	1	neg	0	83	0	291	0	194
	NT	NT	NT	NT	3	neg	0	382	0	805	2	380
	NT	NT	NT	NT	0	neg	1	97	0	138	1	501
	NT	NT	NT	NT	1	neg	5	96	4	1162	0	1115
	NT	NT	NT	NT	2	neg	1	328	NT	NT	0	596
ChAd4DE1gag	NT	NT	1	neg	0	neg	0	0	NT	NT	NT	NT
	NT	NT	0	neg	0	neg	0	159	NT	NT	NT	NT
	NT	NT	0	neg	0	neg	0	1	NT	NT	NT	NT
	NT	NT	1	neg	0	neg	0	234	NT	NT	NT	NT
	NT	NT	1	neg	0	neg	1	0	NT	NT	NT	NT
ChAd16DE1gag	NT	NT	0	neg	0	neg	0	243	NT	NT	NT	NT
	NT	NT	0	neg	0	neg	1	296	NT	NT	NT	NT
	NT	NT	0	neg	2	neg	1	68	NT	NT	NT	NT
	NT	NT	0	neg	0	neg	1	433	NT	NT	NT	NT
	NT	NT	1	neg	0	neg	1	28	NT	NT	NT	NT

EXAMPLE 5 ChAd3 AND CV33 GAG VECTORS ELICIT A CMI RESPONSE CHARACTERIZED BY GAG-SPECIFIC CD8+ T CELLS

In order to characterize the CMI response elicited in response to the ChAd vectors comprising HIV gag transgene, splenocytes pooled from cohorts of five mice immunized with different doses of vector were analyzed by intracellular IFN-γ staining. The data shown in table 3 and table 4 were collected in separate experiments.

Splenocytes were diluted at $2X10^6$ cells in 1 ml of R10 and stimulated with the same antigens described above at the concentration of 2 μg/ml. As controls, DMSO and SEB (Staphylococcal Enterotoxin B) were used. After an o/n incubation in the CO_2 incubator, cells were washed with FACS buffer (1% FCS, 0.01% NaN3, PBS) and purified anti-mouse CD16/CD32 Fc block (clone 2.4G2, Pharmingen cat. 553142) was diluted 1/25, added in the amount of 100 μl/sample and incubated for 15min at 4^0C. Cells were washed in FACS buffer and APC conjugated anti-mouse CD3e (clone 145-2C11, Pharmingen #553066), PE conjugated anti-mouse CD4 (clone L3T4, BD Pharmingen cat. 553142) and PerCP conjugated anti-mouse CD8a (clone 53-6.7, Pharmingen cat. 553036) diluted 1:50 in FACS buffer were added in the amount of 100 μl/sample. Cells were incubated 30 min rt, washed, fixed and permeabilized (Becton Dickinson, FACS Perm 2) and incubated with FITC conjugated anti-mouse IFN- γ Pharmingen cat.554411) diluted 1:50 in PermWash (100 ul/sample) for 30 min at RT. After washing cells were resuspended in 500 ul 1% formaldehyde/PBS and analyzed on a FACS-Calibur flow cytometer, using CellQuest software (Becton Dickinson).

Table 4 provides data summarizing the percentage of gag-specific CD3+T cells that were either gag-specific CD8+ or CD4+ T cells. Positive results are reported in bold. The data provided herein indicate that the cellular profile of the immune response elicited by ChAd vectors derived from viruses classified into different serotype subgroups (i.e., subgroups C, D and E) are similar and all of the gag-specific responses characterized predominantly by CD8+ T cells. In addition, it is noted that at high vector doses a gag-specific CD4+ response becomes evident in all immunization experiments. The ICS assay confirmed that ChAd3 vector can stimulate anti-gag CD8+ response at 10^6 vector dose.

Table 4. Characterization of gag-specific T cells in mice immunized with Chimp adenovirus vectors of different subgroups.

vaccine		10^5		10^6		10^7		10^8		10^9	
		DMSO	gag	DMSO	gag	DMSO	gag	DMSO	gag	DMSO	gag
ChAd3DE1gag	%CD8+CD3+	NT	NT	0.01%	4.65%	0.01%	17.15%	0.04%	24.71%	NT	NT
	%CD4+CD3+	NT	NT	0.00%	0.07%	0.03%	0.08%	0.04%	0.28%	NT	NT
CV33DE1gag	%CD8+CD3+	NT	NT	0.02%	0.01%	0.01%	0.83%	0.03%	8.69%	NT	NT
	%CD4+CD3+	NT	NT	0.00%	0.00%	0.00%	0.04%	0.01%	0.10%	NT	NT
ChAd9DE1gag	%CD8+CD3+	NT	NT	0.02%	0.01%	0.01%	0.68%	NT	NT	0.04%	4.73%
	%CD4+CD3+	NT	NT	0.00%	0.00%	0.00%	0.00%	NT	NT	0.00%	0.01%
ChAd10DE1gag	%CD8+CD3+	NT	NT	0.02%	0.01%	0.01%	0.57%	NT	NT	0.02%	5.04%
	%CD4+CD3+	NT	NT	0.00%	0.00%	0.00%	0.00%	NT	NT	0.00%	0.01%
ChAd6DE1gag	%CD8+CD3+	NT	NT	0.00%	0.01%	0.00%	0.59%	0.01%	14.28%	NT	NT
	%CD4+CD3+	NT	NT	0.00%	0.00%	0.00%	0.05%	0.01%	0.12%	NT	NT
ChAd7DE1gag	%CD8+CD3+	NT	NT	0.01%	0.02%	0.01%	0.00%	0.02%	5.00%	NT	NT
	%CD4+CD3+	NT	NT	0.00%	0.01%	0.00%	0.00%	0.01%	0.21%	NT	NT

EXAMPE 6 ChAd VECTORS ELICIT HCV NS-SPECIFIC T CELL RESPONSE

The potency of CV32-NSmut and CV33-NSmut vectors was evaluated in C57/Black6 mice relative to the potency of MRKAd6NSmut. The animals were injected with 10-fold increasing doses of vector starting from 10^7 up to 10^9 vp/mouse. CMI was analyzed 3 weeks after a single injection by IFN-γ ELISPOT and IFN-γ intracellular staining by stimulating T cells with a 9-mer peptide reproducing a CD8+ T cell epitope mapped in the helicase domain of NS3 protein. The data provided in Table 5 summarize the number of spot-forming cells per million splenocytes following incubation in absence (mock) or in presence of NS3 9-mer peptide.

The data indicate that both CV32 and CV33 vectors expressing HCV-NS stimulate strong T cell responses. Based on the observation that the first positive result for the CV32 vector was obtained by injecting 10^9 vp/dose, the immunization potency of CV32DE1E3 NSmut vector appears to be approximately 100-fold lower than human subgroup C Ad6DE1E3 NSmut vector. The parallel experiment with MRKAd6NSmut indicated that a dose of 10^7 vp/animal was sufficient to stimulate cell mediated immunity. Therefore, these results confirm the lower immunization potency of CV32-derived vectors relative to human subgroup C vectors

(such as hAd5 and hAd6) that was also observed in the experiment with gag expressing vectors (see Table 3).

Table 5. HCV NS-specific T cell response in mice immunized with MRKAd6 NSmut, CV32NSmut or CV33NSmut

Vaccination	10^7 vp		10^8 vp		10^9 vp		10^10 vp	
	Mock	NS3	mock	NS3	mock	NS3	mock	NS3
MRKAd6NSmut	1	345	1	449	NT	NT	NT	NT
	1	248	1	1590	NT	NT	NT	NT
	1	1	1	549	NT	NT	NT	NT
	1	262			NT	NT	NT	NT
					NT	NT	NT	NT
CV33NSmut	1	1	1	195	2	338	NT	NT
	1	2	1	409	1	1136	NT	NT
	1	1	1	396	1	497	NT	NT
	1	2	2	172	1	344	NT	NT
	1	237			1	163	NT	NT
CV32NSmut	neg	neg	1	181	1	118	1	176
	neg	neg	1	71	1	239	1	238
	neg	neg	1	56	1	862	1	555
	neg	neg	1	459	1	219	1	545
	neg	neg	1	195	1	123	1	578

EXAMPLE 7 ANTI -Ad5 PRE-EXISTING IMMUNITY DOES NOT ABROGATE ANTI-GAG CMI ELICITED BY ChAd3gag

To evaluate the impact on ChAd3 immunization of the pre-existing immunity against the high seroprevalent Ad5, 4 cohorts of 5 BalbC mice were pre-immunized with two injection of 10^{10} vp of Ad5 wt in the quadriceps at week 0 and 2. As control, 2 cohorts of 5 mice were injected at the same time points with buffer only. Cohorts of Ad5 pre-immunized mice were then immunized with 10^6 and 10^7 vp/mouse of either Ad5gag or ChAd3gag vectors. Cohorts of control (naïve) mice were immunized with 106 vp/mouse of Ad5gag or ChAd3gag vectors. Anti-Ad5 and ChAd3 neutralizing immunity was evaluated at week 4 by the neutralization assay described above using Ad5 and ChAd3 SEAP vectors. Anti-gag immunity was evaluated by ELISPOT analysis on purified splenocytes stimulated with gag 9-mer peptide containing a gag epitope mapped in BalbC mice. The results reported in figure 36 demonstrated that Anti-Ad5 immunity does not abrogate anti-gag CMI elicited by ChAd3gag while, as expected, anti-Ad5 immunity completely block Ad5gag immunization.

EXAMPLE 8 ChAd3hCEA IMMUNIZATION ELICITS A STRONG CEA-SPECIFIC IMMUNE RESPONSE IN TRANSGENIC MICE EXPRESSING HUMAN CEA

The ability of the ChAd vectors disclosed and claimed herein to elicit an immune response against a self-antigen therefore breaking the tolerance was also evaluated in transgenic mice expressing human CEA (Clarke, P *et al. Cancer Res.* (1998) 58(7):1469-77.)

Cohorts of 8 mice were injected in the quadriceps with 10^10 vp of ChAd3hCEA or Ad5hCEA as already described. The immune response against CEA was followed weekly up to day 75 on PBMC stimulated with a pool of 15-mer peptides encompassing human CEA aminoacid sequence from aa 497 to the end (aa 703). Anti-CEA immunity was evaluated by ICS determining CD4-CD8+ T cells secreting interferon-γ in response to CEA peptide pool incubation.

The results reported in figure 37 demonstrate that ChAd3hCEA vector immunization stimulate a more sustained CD8+ T cell response against human CEA than Ad5 expressing the same transgene.

PRIMATE IMMUNIZATION STUDIES

METHODS AND MATERIALS

Immunization Protocol

The ability of the ChAd vectors disclosed and claimed herein to elicit CMI in Rhesus macaques (referred to herein as monkeys) was also evaluated. The macaques were anesthetized (ketamine/xylazine) and the vaccines were delivered i.m. in 0.5-mL aliquots into both deltoid muscles using tuberculin syringes (Becton-Dickinson). In all cases the macaques were between 3-10 kg in weight, and the total dose of each vaccine was administered in 1 mL of buffer.

Sera and peripheral blood mononuclear cells (PBMC) were prepared from blood samples collected at several time points during the immunization regimen. All animal care and treatment were in accordance with standards approved by the Institutional Animal Care and Use Committee according to the principles set forth in the *Guide for Care and Use of Laboratory Animals*, Institute of Laboratory Animal Resources, National Research Council.

ELISPOT Assay

The IFN-γ ELISPOT assays for rhesus macaques were conducted following a previously described protocol (Allen *et al.*, 2001 *J. Virol.* 75(2):738-749), with some modifications. For gag-specific stimulation, a peptide pool was prepared from 20-aa peptides that encompass the entire HIV-1 gag sequence with 10-aa overlaps (Synpep Corp., Dublin, CA). For HCV NS-specific stimulation 6 peptide pools were prepared from 15-aa peptides that encompass the entire HCV-NS sequence from NS3 to NS5b with 10-aa overlaps.
HER2/neu and CEA-specific stimulations were performed with 15-aa peptides that encompass the entire protein sequence with 10-aa overlaps.

To each well, 50 µL of 2-4 x 10^5 peripheral blood mononuclear cells (PBMCs) were added; the cells were counted using Beckman Coulter Z2 particle analyzer with a lower size cut-off set at 80 fL. Either 50 µL of media or the gag peptide pool at 8 µg/mL concentration per peptide was added to the PBMC. The samples were incubated at 37°C, 5% CO_2 for 20-24 hrs. Spots were developed accordingly and the plates were processed using custom-built imager and automatic counting subroutine based on the ImagePro platform (Silver Spring, MD); the counts were normalized to 10^6 cell input.

Intracellular Cytokine Staining (ICS)

To 1 ml of 2 x 10^6 PBMC/mL in complete RPMI media (in 17x100mm round bottom polypropylene tubes (Sarstedt, Newton, NC)), anti-hCD28 (clone L293, Becton-Dickinson) and anti-hCD49d (clone L25, Becton-Dickinson) monoclonal antibodies were added to a final concentration of 1 µg/mL. For gag-specific stimulation, 10 µL of the peptide pool (at 0.4 mg/mL per peptide) were added. Similar conditions were used for HCV NS-specific stimulation. The tubes were incubated at 37 °C for 1 hr., after which 20 µL of 5 mg/mL of brefeldin A (Sigma) were added. The cells were incubated for 16 hr at 37 °C, 5% CO_2, 90% humidity. 4 mL cold PBS/2%FBS were added to each tube and the cells were pelleted for 10 min at 1200 rpm. The cells were re-suspended in PBS/2%FBS and stained (30 min, 4 °C) for surface markers using several fluorescent-tagged mAbs: 20 µL per tube anti-hCD3-APC, clone FN-18 (Biosource); 20 µL anti-hCD8-PerCP, clone SK1 (Becton Dickinson, Franklin Lakes, NJ); and 20 µL anti-hCD4-PE, clone SK3 (Becton Dickinson). Sample handling from this stage was conducted in the dark. The cells were washed and incubated in 750 µL 1xFACS Perm buffer (Becton Dickinson) for 10 min at room temperature. The cells were pelleted and re-suspended in PBS/2%FBS and 0.1 µg of FITC-anti-hIFN-γ, clone MD-1 (Biosource) was added. After 30 min incubation, the cells were washed and re-suspended in PBS. Samples were analyzed using all four color channels of the Becton Dickinson FACSCalibur instrument. To

analyze the data, the low side- and forward-scatter lymphocyte population was initially gated; a common fluorescence cut-off for cytokine-positive events was used for both $CD4^+$ and $CD8^+$ populations, and for both mock and gag-peptide reaction tubes of a sample.

EXAMPLE 9 A HOMOLOGOUS PRIME-BOOST REGIMEN USING ChAd ΔE1-gag VECTORS ELICITS GAG-SPECIFIC T CELLS IN MONKEYS

Cohorts of 3 animals were given intramuscular injection at week 0 and week 4 of either of the following constructs: 10^10 vp of CV-32ΔE1-gag; or 10^10 vp CV33ΔE1-gag; or 10^10 vp and 10^8 vp MRKAd5ΔE1gag. PBMCs collected at regular 4-wks intervals were analyzed in an ELISPOT assay. The results provided in Table 6, which indicate the number of spot-forming cells per million PBMC following incubation in absence (mock) or presence of Gag peptide pool establish that both CV32ΔE1-gag and CV-33ΔE1gag are able to induce significant levels of gag-specific T cells in non-human primates. It is interesting to note that after a single dose (wk 4), the CV32ΔE1-gag responses were comparable to MRKAd5 ΔE1-gag 10^8 vp dose and lower than that of MRKAd5-gag 10^10 vp/dose. CV33ΔE1-gag 10^10 vp/dose induces a response comparable to that of MRKAd5-gag 10^10 vp/dose. This result was confirmed at week 8 after the second dose.

Table 6. Gag-specific T cell response in monkeys immunized with MRKAd5 ΔE1-gag, CV32ΔE1-gag, CV33ΔE1-gag.

Vaccination T=0	vector dose	Monk #	Pre-bleed		T=4		T=8	
			Mock	Gag	Mock	Gag	Mock	Gag
CV32ΔE1gag	10^10 vp	01C023	1	0	14	353	3	278
		01C029	1	3	13	605	3	419
		01C032	1	0	5	274	1	179
CV33ΔE1gag	10^10 vp	01C033	0	0	9	1545	1	659
		01C036	4	5	4	1540	13	881
		01D303	0	3	19	949	10	628
MRKAd5gag	10^8 vp	01D267	0	0	4	473	0	341
		01D279	1	4	44	831	6	336
		01D284	4	5	4	264	5	129
MRKAd5gag	10^10 vp	99C218	0	3	5	2500	0	1580
		99C227	6	1	4	529	5	365
		99D185	ND	ND	0	425	0	310

EXAMPLE 10 ChAd VECTORS ELICIT A HCV NS-SPECIFIC T-CELL RESPONSE IN A HETEROLOGOUS PRIME-BOOST REGIMEN

In a separate experiment, groups of two and three monkeys were given immunization at week 0, 4 of MRK Ad6NSoptmut vector at 10^8 or 10^10 vp per animal. The animals were boosted with the same virus at the same dose at week 24 and then boosted again at week 104 with CV33-NSmut at 10^10 vp per animal. The results are presented in Tables 7 and 8 which summarize the number of spot-forming cells per million PBMC following incubation in absence (mock) or presence of HCV NS peptide pool.

T cell immunity, as assessed by IFN-γ ELISPOT, showed a peak response at week 4 after the first dose in the animals injected with 10^10 vp (Table 8) and at week 8 (post-dose 2) in the animals injected at 10^8 (Table 7). The response was not boosted by the injection at week 24 ("homologous boost"), while a strong boost effect was observed after the injection with CV33-NSmut ("heterologous boost").

Table 7. HCV NS-specific T cell response in monkeys immunized with MRK Ad6NSoptmut at 10^8 vp/animal and boosted with CV33-NSmut.

Vaccine	MRKAd6NSoptmut 10^8 vp								CV33-NSmut 10^10 vp			
time point	post-priming I dose T=4		post-priming II dose T=8		pre-homologous boost T=24		post-homologous boost T=28		pre-heterologous boost T=104		post-heterologous boost T=108	
monkey	*95116*	*138T*	*95116*	*138T*	*95116*	*138T*	*95116*	*138T*	*95116*	*138T*	*95116*	*138T*
poolF	44	112	77	124	115	176	105	55	120	150	188	2228
poolG	20	2110	66	1975	201	1105	94	884	120	192	96	4590
poolH	12	18	54	22	169	221	28	9	81	33	447	543
poolI	14	53	62	47	163	189	96	18	80	67	71	515
poolL	33	88	58	44	353	608	235	33	110	131	224	308
poolM	184	75	168	138	204	336	67	44	55	46	2028	1570
DMSO	14	3	44	7	104	79	33	6	57	40	33	65

Table 8. HCV NS-specific T cell response in monkeys immunized MRK Ad6NSoptmut at and 10^10 vp/animal and boosted with CV33-NSmut.

Vaccine	MRKAd6NSoptmut 10^10 vp												CV33-NSmut 10^10					
time point	post-priming I dose T=4			post-priming II dose T=8			pre-homologous boost T=24			post-homologous boost T=28			pre-heterologous boost T=104			post-heterologous boost T=108		
monkey	*98D209*	*106Q*	*113Q*	*98D209*	*106Q*	*113Q*	*98D209*	*106Q*	*113Q*	*98D209*	*106Q*	*113Q*	*98D209*	*106Q*	*113Q*	*98D209*	*106Q*	*113Q*
poolF	3110	263	404	1340	300	723	678	61	583	321	123	1438	204	192	326	1581	1525	1714
poolG	2115	642	1008	1070	316	2205	685	71	701	251	178	1758	166	106	625	1118	524	4238
poolH	373	72	19	358	43	43	424	24	42	51	23	18	92	45	55	413	58	211
poolI	103	37	347	80	36	531	237	39	169	12	35	485	66	79	376	459	85	2738
poolL	149	22	10	93	36	29	279	46	48	11	49	51	89	109	73	199	76	431
poolM	314	428	19	153	243	20	333	81	38	38	134	11	41	81	9	228	1440	227
DMSO	0	1	3	16	16	5	128	8	9	8	10	16	20	51	12	18	13	5

The efficiency of heterologous boost with chimp Ad vectors was evaluated in a second experiment. Cohorts of three monkeys were immunized at week 0 and week 4 with MRKAd5gag (10^10 vp/animal), MRKAd6NSmut (10^10 vp/animal) or with the combination of both vectors (10^10 vp/animal each vector) then boosted with the same immunogen at week 24 (homologous boost). Homologous boost was performed with the same immunogens; heterologous boost was performed with CV33gag, CV32 NSmut or with the two vectors in combination. The results provided in Table 9 summarize the number of spot-forming cells per million PBMC following incubation in absence (mock) or presence of HCV NS peptide pool.

The same cohorts were boosted again at week 51 with CV33gag (10^10 vp/animal), CV32NSmut (10^10 vp/animal) and with the combination of the two vectors (10^10 vp/animal each vector). The results provided in Table 9 further indicate that the homologous boost was not efficient since the responses are below the peak observed at week 4 after the injection of the first dose of vaccine. A strong boosting effect was measured by IFN-γ ELISPOT at week 54 after immunization with heterologous chimp vectors.

Table 9. Immunization with Chimp Ad vectors efficiently boost Gag and HCV NS-specific T cell response in monkeys immunized with MRK Ad5gag or MRK Ad6NSoptmut at 10^10 vp/animal.

Vaccine	MRKAd5gag												CV33gag					
time point	post-dose 1 (T=4)			post-dose 2 (T=8)			pre-homol. boost (T=24)			post-homol. boost (T=28)			pre-heterol. boost (T=51)			post-heterol. boost (T=54)		
animal ID	00D105	00D076	00D299	00D105	00D076	00D299	00D105	00D076	00D299	00D105	00D076	00D299	00D105	00D076	00D299	00D105	00D076	00D299
poolF	18	35	60	16	29	14	37	76	40	37	8	14	37	27	44	43	44	70
poolG	16	23	49	4	28	31	54	95	106	81	2	46	36	27	37	84	108	109
poolH	45	51	57	18	31	42	55	88	55	47	11	32	69	36	60	85	58	120
pooll	21	21	48	4	26	11	19	54	26	38	6	6	22	11	32	33	26	24
poolL	15	21	58	9	31	20	71	183	128	106	6	27	61	21	65	28	45	44
poolM	39	24	49	26	14	49	38	93	39	59	6	19	62	23	38	27	19	14
Gag	1764	2208	2762	574	1906	1959	391	935	702	2123	336	736	485	833	1384	4003	4333	3863
DMSO	9	13	37	7	14	13	16	76	33	26	3	11	28	19	39	23	16	53

Vaccine	MRK Ad5gag + MRKAd6NSmut												CV33gag + CV32NSmut					
time point	post-dose 1 (T=4)			post-dose 2 (T=8)			pre-homol. boost (T=24)			post-homol. boost (T=28)			pre-heterol. boost (T=51)			post-heterol. boost (T=54)		
animal ID	00D088	00D099	00D240	00D088	00D099	00D240	00D088	00D099	00D240	00D088	00D099	00D240	00D088	00D099	00D240	00D088	00D099	00D240
poolF	438	118	105	720	116	154	206	108	242	408	99	219	778	135	56	1701	1121	424
poolG	21	784	1483	44	362	940	19	234	548	47	781	844	78	363	265	228	3180	2770
poolH	24	53	8	46	27	19	13	66	93	49	41	87	115	50	28	97	291	104
pooll	83	28	9	90	24	8	16	40	68	33	16	42	56	19	8	165	145	22
poolL	13	14	13	16	17	9	28	101	140	39	27	78	59	28	15	137	815	463
poolM	39	31	6	101	27	16	21	73	107	44	26	78	114	28	10	219	109	21
Gag	2138	1044	1063	2260	505	819	454	241	456	1100	368	716	1542	237	161	4460	2908	1764
DMSO	5	6	3	8	5	1	10	18	43	9	13	28	14	18	12	9	21	6

Vaccine	MRKAd6 NSmut												CV32NSmut					
time point	post-dose 1 (T=4)			post-dose 2 (T=8)			pre-homol. boost (T=24)			post-homol. boost (T=28)			pre-heterol. boost (T=51)			post-heterol. boost (T=54)		
animal ID	00D065	00D116	00D159	00D065	00D116	00D159	00D065	00D116	00D159	00D065	00D116	00D159	00D065	00D116	00D159	00D065	00D116	00D159
poolF	139	44	82	92	121	63	62	116	54	44	42	23	57	85	53	313	385	261
poolG	154	253	119	77	156	108	93	165	125	104	59	39	44	198	48	196	764	559
poolH	1284	41	211	768	35	124	394	84	77	24	817	48	624	31	116	3758	90	925
pooll	302	22	1174	221	16	1069	134	31	561	18	133	478	84	16	362	485	51	2951
poolL	28	16	48	35	32	21	141	113	78	19	48	17	46	33	46	379	339	541
poolM	1329	1007	36	579	392	30	314	293	43	558	398	22	159	369	33	1278	1750	16
Gag	15	9	7	13	5	2	36	33	36	9	23	14	16	8	10	37	9	26
DMSO	16	4	5	9	6	4	23	17	8	1	9	3	23	8	6	26	9	10

EXAMPLE 11 VACCINATION WITH A ChAd VECTOR COMPRISING A TAA BREAKS TOLERANCE AND ELICITS A TAA-SPECIFIC T CELL RESPONSE IN MONKEYS

Experiments designed to determine whether chimpanzee adenoviral vectors are sufficiently immunogenic to break the tolerance to a self-antigen and to document the utility of chimpanzee vectors for boosting an immune response primed with a human adenoviral vector were performed in cohorts of four monkeys. Animals were immunized with three injection at

week 0, 2 and 4 of Ad5DE1 RhCEA (10^11 vp), comprising the tumor associated antigen CEA, followed by vaccination at week 16, 18 and 20 with CV33DE1 RhCEA (10^11 vp). T cell response was measured by IFNγ ELISPOT with rhesus CEA peptides.

The results reported in figure 34, which provide the number of spot-forming cells per million PBMC following incubation in absence (DMSO) or in presence of rhesus CEA C and D peptides pools, establish that an immunization protocol based on vaccination with two different Ad serotypes leads to a sustained T cell response against CEA in non-human primates.

While the invention has been described in detail with reference to certain preferred embodiments thereof, it will be understood that modifications and variations are within the spirit and scope of that which is described and claimed.

CLAIMS

What is claimed is:

1. An isolated chimpanzee nucleic acid sequence selected from the group consisting of:
   a) SEQ ID NO:1
   b) SEQ ID NO: 2; and
   c) a nucleic acid sequence complementary to the sequence of (a) or (b).

2. An isolated recombinant chimpanzee serotype comprising any combination of hexon and fiber nucleic acid sequences selected from the groups of:
   a) hexon sequences SEQ ID NOS: 16- 25; and
   b) fiber sequences SEQ ID NOS: 6-15. ,

3. A replication defective chimpanzee adenoviral (ChAd) vector comprising the nucleotide sequence set forth in SEQ ID NO:1 or SEQ ID NO:2 and a transgene which encodes at least one immunogen operatively linked to regulatory sequences which direct expression of said transgene in mammalian cells, wherein said vector lacks the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:2 which comprises at least one gene selected from the group consisting of adenoviral E1, E2, E3, and E4.

4. A replication defective ChAd vector which comprises a deletion/disruption in the E1 nucleotide sequence in the region from bp 460 to bp 3542 of SEQ ID NO: 1 or from bp 457 to bp 3425 of SEQ ID NO:2.

5. The ChAd vector according to claim 4, wherein the vector comprises a transgene selected from the group consisting of: HIV, HBV, HCV, HPV, HSV1, HSV2, SARS CoV, *Plasmodium malariae*, Ebola virus, West Nile virus, Dengue virus, Influenza A, Influenza B, and *Mycobacterium tubercolosis.*

6. The ChAd vector according to claim 4, wherein the vector comprises a deletion/disruption in the E1 nucleotide sequence in the region from bp 460 to bp 3542 of SEQ ID NO: 1 or from bp 457 to bp 3425 of SEQ ID NO:2 and further wherein the vector comprises a transgene encoding at least one tumor associated antigen (TAA).

7. The ChAd vector according to claim 6 wherein the at least one TAA is selected from the group consisting of: HER2 NEU, CEA, EPCAM, PSA, PSMA, TELOMERASE, GP100, MELAN-A/MART-1, MUC-1, NY-ESO-1, SURVIVIN, STROMELYSIN 3, TYROSINASE, MAGE3, CML68, CML66, OY-TES-1, SSX-2, SART-1, SART-2, SART-3, NY-CO-58, NY-BR-62, HKLP2, 5T4 and VEGFR2.

8. A host cell comprising a nucleic acid molecule according to claim 1 or claim 2, wherein said host cell expresses one or more adenoviral regions selected from the group consisting of E1a, E1b, E2a, E2b, E4 orfs 1, 2, 3, 4, 5, 6, 6/7, pIX, IVa2, regions L1, L2, L3, L4, L5.

9. A method of producing a replication-defective chimpanzee adenoviral vector comprising introducing an adenoviral vector according to Claims 3 into an adenoviral E-1 expressing human cell, and harvesting the resulting adenoviruses.

10. The method according to Claim 9, wherein the human cell is a 293 cell or a PER.C6™ cell.

11. A vaccine composition comprising a replication-defective ChAd vector according to any one of Claims 3-7.

12. An adenoviral E1-expressing human cell comprising the nucleotide sequence set forth in SEQ ID NO:1.

13. An adenoviral E1-expressing human cell comprising the nucleotide sequence set forth in SEQ ID NO: 2.

14. A method of boosting an antigen-specific immune response in a mammal comprising administering to said mammal a sufficient amount of a recombinant ChAd vector comprising a chimpanzee adenovirus genome containing at least a functional deletion of its E1 gene, a nucleotide sequence encoding a target antigen and a promoter sequence capable of directing expression of the nucleotide sequence encoding the target antigen, wherein administration of said chAd vector elicits a boosted response.

15. The method of claim 14, wherein the ChAd vector comprises a complete deletion of its E1 genes and further wherein the vector optionally comprises a deletion of its E3 genes.

16. The method of claim 14, wherein the boosted immune response is specific for an antigen derived from an infectious agent selected from the group consisting of: HIV, HBV, HCV, HPV, HSV1, HSV2, SARS CoV, *Plasmodium malariae*, Ebola virus, West Nile virus, Dengue virus, Influenza A, Influenza B, and *Mycobacterium tubercolosis*.

17. The method of claim 14, wherein the immune response is a boosted immune response that is specific for a TAA.

18. The method of claim 17, wherein the boosted immune response comprises the production of antigen-specific CD8+ T cells.

19. The method of claim 14, wherein the boosted immune response comprises the production of antigen-specific CD8+ T cells.

20. A method of eliciting an immune response in a naïve mammal comprising administering to said mammal a sufficient amount of a ChAd vector which comprises a chimpanzee adenovirus genome containing at least a functional deletion of its E1 gene, a nucleotide encoding a target antigen and a promoter sequence capable of directing expression of the nucleotide sequence encoding the target antigen, wherein administration of the ChAd vector elicits a primary immune response.

21. The method of claim 20, wherein the primary immune response is specific for an antigen derived from an infectious agent such as, but not limited to HIV, HCV, HPV, HSV1, HSV2, SARS CoV, *Plasmodium malariae*, Ebola virus, West Nile virus, Dengue virus, Influenza A, Influenza B, *Mycobacterium tubercolosis*.

22. The method of claim 14, wherein the immune response is a primary immune response that is specific for a TAA against which the mammal is tolerant.

23. A method of claim according to any one of claims 14 to 22, wherein the recombinant adenovirus comprises a nucleotide sequence encoding a hexon peptide selected from the group consisting of: SEQ ID NOS: 14-21.

24. A method of claim according to any one of claims 14 to 22,, wherein the recombinant adenovirus comprises a nucleotide sequence encoding a fiber protein sequence selected from the group consisting of: SEQ ID NOS: 6-15.

25. A method of inducing an immune response against an antigen derived from an infectious agent selected from the group consisting of: HIV, HCV, HPV, HSV1, HSV2, SARS, *Plasmodium maleriae*, Ebola virus, West Nile virus, Dengue virus, Influenza A, Influenza B, and *Mycobacterium tubercolosis* comprising: (a) priming a host to respond to a infectious agent-antigen by administering a first vaccine composition comprising a nucleotide sequence encoding a infectious agent-antigen against which an antigen-specific immune response is desired; and (b) boosting the immune response of step (a) by administering a second vaccine composition comprising a recombinant ChAd vector containing at least a functional deletion of its E1 gene, and in the site of the E1 gene deletion, a sequence comprising a promoter capable of directing expression of DNA encoding the same infectious agent–antigen delivered in the priming step,
wherein administration of the boosting composition elicits an immune response which has the effect of conferring protective immunity.

26. The method according to claim 25, wherein the first vaccine composition comprises plasmid DNA which is administered intramuscularly in combination with electrical stimulation.

27. The method of claim 25, wherein the second vaccine composition comprises a ChAd vector comprising DNA encoding an antigen derived from an infectious agent selected from the group consisting of: HIV, HCV, HPV, HSV1, HSV2, SARS, Malaria, Ebola virus, West Nile virus, Dengue virus, Influenza A, Influenza B, and *Mycobacterium tubercolosis*.

28. The method of Claim 27, wherein the immune response comprises the production of antigen-specific CD8+ T cells.

29. The method of claim 27, wherein the ChAd vector is selected from the group consisting of: ChAd3, ChAd6, ChAd20, ChAd4, ChAd5, ChAd7, ChAd9, ChAd10, ChAd11, ChAd 16, ChAd17, and ChAd19.

30. The method of claim 25, wherein the ChAd vector comprises a nucelotide sequence encoding a hexon peptide selected from the group consisting of: SEQ ID NO: 16-25.

31. The method of claim 25, wherein the ChAd vector comprises a nucelotide sequence encoding a fiber peptide selected from the group consisting of: SEQ ID NOS: 6-15.

32. The method of claim 25, wherein the first and second vaccine compositions are both ChAd vectors characterized by different serotypes.

33. A method of breaking host tolerance to a self-antigen comprising: (a) priming a host to respond to a self-antigen by administering a first vaccine composition comprising a nucleotide sequence encoding a self-antigen against which an antigen-specific immune response is desired, thereby eliciting a primed response; and (b) boosting the primed immune response of step (a) by administering a second vaccine composition comprising a recombinant ChAd vector containing at least a functional deletion of its E1 gene, and in the site of the E1 gene deletion, a sequence comprising a promoter capable of directing expression of DNA encoding the same self-antigen delivered in the priming step, wherein administration of the boosting composition elicits an immune response which has the effect of breaking host tolerance to the self-antigen.

34. The method according to claim 33, wherein the first vaccine composition comprises plasmid DNA which is administered intramuscularly in combination with electrical stimulation.

35. The method of claim 33, wherein the second vaccine composition comprises a ChAd vector comprising DNA encoding a self antigen selected from the group consisting of: HER2 NEU, CEA, HEPCAM, PSA, PSMA, TELOMERASE, GP100, MELAN-A/MART-1, MUC-1, NY-ESO-1, SURVIVIN, STROMELYSIN 3, TYROSINASE, MAGE3, CML68, CML66, OY-TES-1, SSX-2, SART-1, SART-2, SART-3, NY-CO-58, NY-BR-62, HKLP2, 5T4 and VEGFR2.

36. The method of Claim 35, wherein the immune response comprises the production of antigen-specific CD8+ T cells.

37. The method of claim 35, wherein the ChAd vector is selected from the group consisting of: ChAd3, ChAd6, ChAd20, ChAd4, ChAd5, ChAd7, ChAd9, ChAd10, ChAd11, ChAd16, ChAd17, and ChAd19.

38. The method of claim 35, wherein the ChAd vector comprises a nucleotide sequence encoding a hexon peptide selected from the group consisting of: SEQ ID NO: 16-25.

39. The method of claim 35, wherein the ChAd vector comprises a nucleotide sequence encoding a fiber peptide selected from the group consisting of: SEQ ID NOS: 6-15.

40. The method of claim 35, wherein the first and second vaccine compositions are both ChAd vectors characterized by different serotypes.

41. The method of claim 35, wherein the host is a tumor-bearing mammal who has developed resistance to cancer chemotherapy.

ABSTRACT OF THE DISCLOSURE

The present invention provides recombinant replication-defective adenoviral vectors derived from chimpanzee adenoviruses and methods for generating recombinant adenoviruses in human E1-expressing cell lines. The invention also provides compositions and methods suitable for use for the delivery and expression of transgenes encoding immunogens against which a boosted immune response is desired. The invention further provides methods of generating clinical grade vector stocks suitable for use in humans. In a particular embodiment the invention contemplates the use of vectors comprising transgenes which encode tumor associated antigens in vaccines and pharmaceutical compositions for the prevention and treatment of cancer.

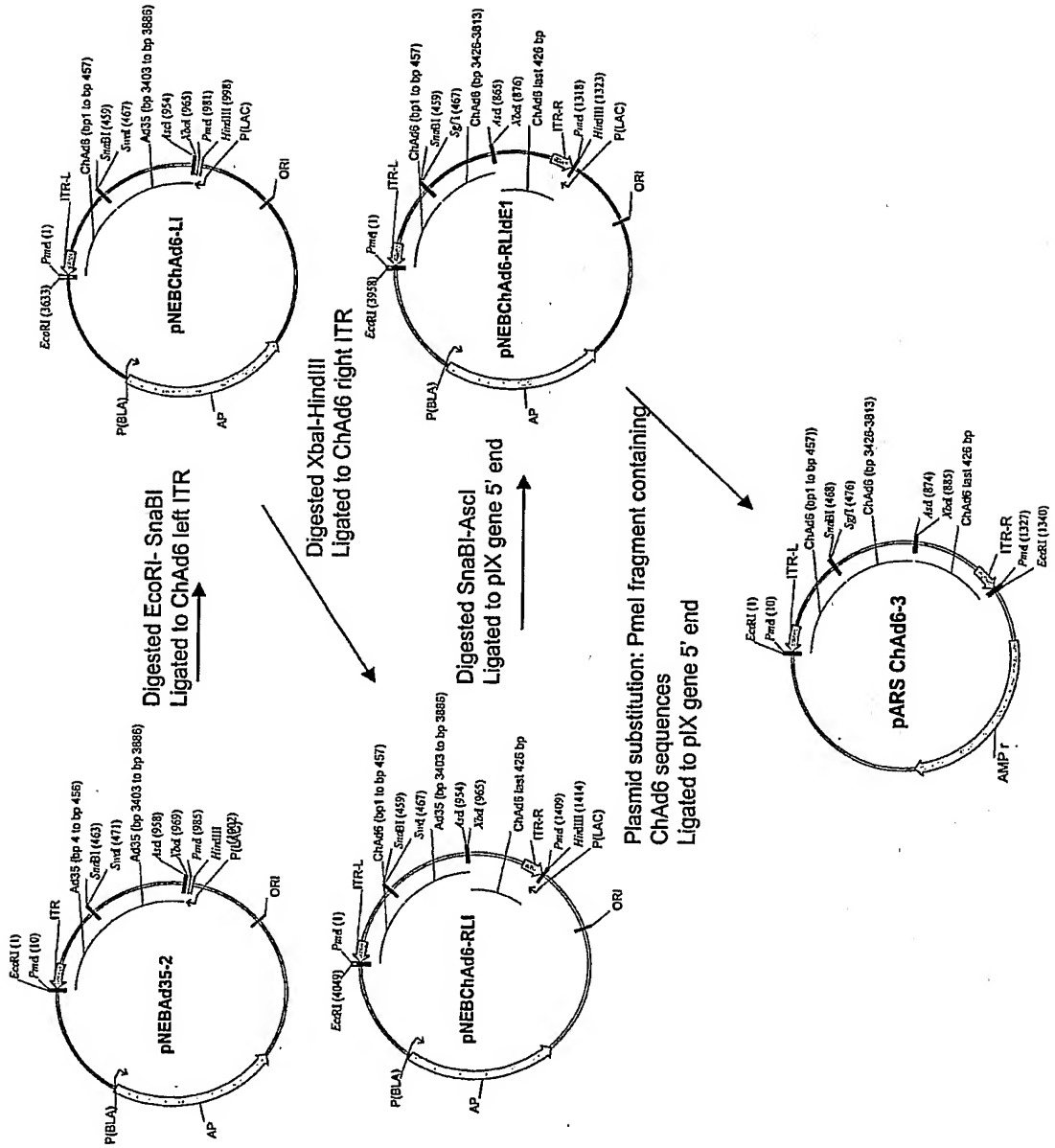

Fig. 1

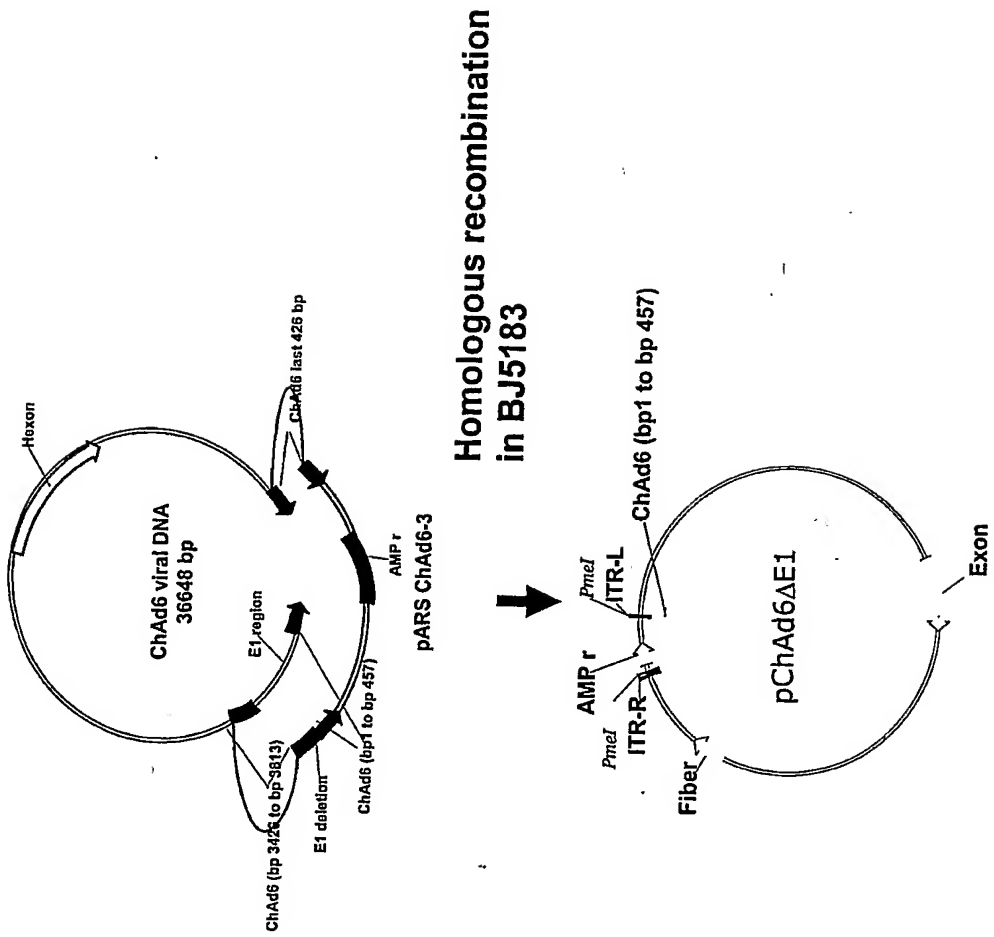

Fig. 2

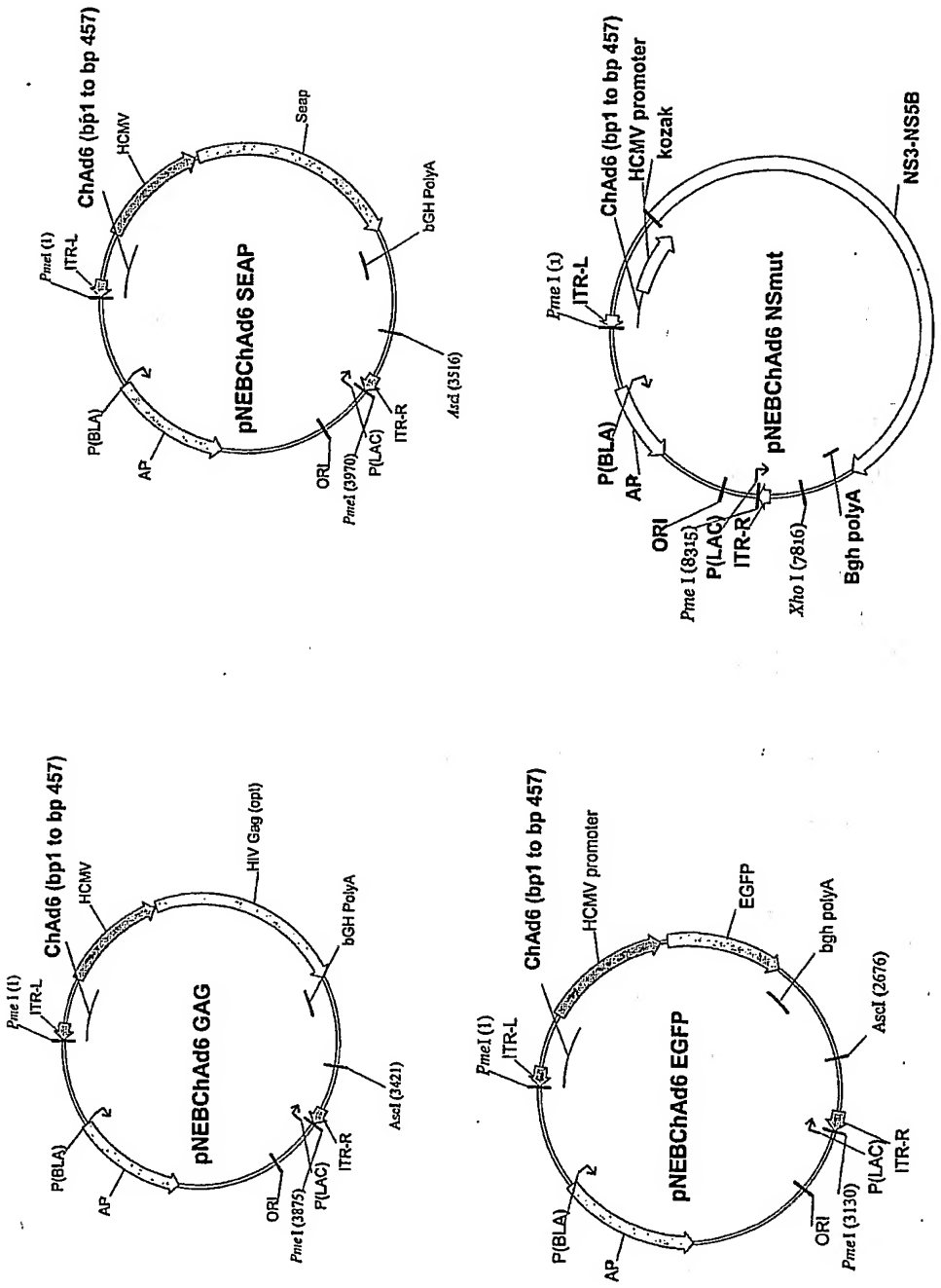

Fig. 3

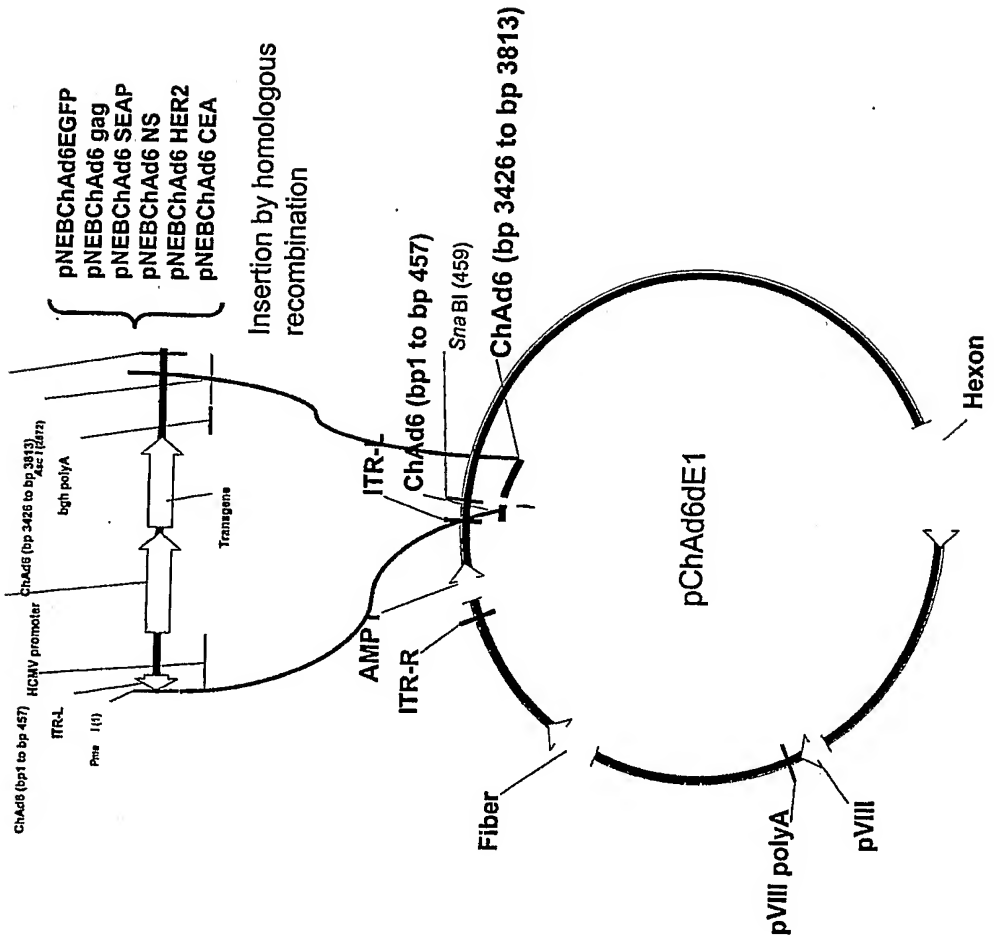

Fig. 4

SEQ ID NO:1


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  61  CGAGGCGGGG CGCGGGGCGG GAGGCGGGTT TGGGGGCGGG CCGGCGGGCG GGGCGGTGTG
 121  GCGGAAGTGG ACTTTGTAAG TGTGGCGGAT GTGACTTGCT AGTGCCGGGC GCGGTAAAAG
 181  TGACGTTTTC CGTGCGCGAC AACGCCCCCG GGAAGTGACA TTTTTCCCGC GGTTTTTACC
 241  GGATGTTGTA GTGAATTTGG GCGTAACCAA GTAAGATTTG GCCATTTTCG CGGGAAAACT
 301  GAAACGGGGA AGTGAAATCT GATTAATTTT GCGTTAGTCA TACCGCGTAA TATTTGTCTA
 361  GGGCCGAGGG ACTTTGGCCG ATTACGTGGA GGACTCGCCC AGGTGTTTTT TGAGGTGAAT
 421  TTCCGCGTTC CGGGTCAAAG TCTCCGTTTT ATTATTATAG TCAGCTGACG CGGAGTGTAT
 481  TTATACCCTC TGATCTCGTC AAGAGGCCAC TCTTGAGTGC CAGCGAGTAG AGTTTTCTCC
 541  TCTGCCGCTC TCCGCTCCGC TCCGCTCGGC TCTGACACCG GGGAAAAAAT GAGACATTTC
 601  ACCTACGATG GCGGTGTGCT CACCGGCCAG CTGGCTGCTG AGGTCCTGGA CACCCTGATC
 661  GAGGAGGTAT TGGCCGATAA TTATCCTCCC TCGACTCCTT TTGAGCCACC TACACTTCAC
 721  GAACTATACG ATCTGGATGT GGTGGGGCCC AGCGATCCGA ACGAGCAGGC GGTTTCCAGT
 781  TTTTTTCCAG AGTCCATGTT GTTGGCCAGC CAGGAGGGGG TCGAACTTGA GACCCCTCCT
 841  CCGATCGTGG ATTCCCCCGA TCCGCCGCAG CTGACTAGGC AGCCCGAGCG CTGTGCGGGA
 901  CCTGAGACTA TGCCCCAGCT GCTACCTGAG GTGATCGATC TCACCTGTAA TGAGTCTGGT
 961  TTTCCACCCA GCGAGGATGA GGACGAAGAG GGTGAGCAGT TTGTGTTAGA TTCTGTGGAA
1021  CAACCCGGGC GAGGATGCAG GTCTTGTCAA TATCACCGGA AAAACACAGG AGACTCCCAG
1081  ATTATGTGTT CTCTGTGTTA TATGAAGATG ACCTGTATGT TTATTTACAG TAAGTTTATC
1141  ATCGGTGGGC AGGTGGGCTA TAGTGTGGGT GGTGGTCTTT GGGGGGTTTT TTAATATATG
1201  TCAGGGGTTA TGCTGAAGAC TTTTTTATTG TGATTTTTAA AGGTCCAGTG TCTGAGCCCG
1261  AGCAAGAACC TGAACCGGAG CCTGAGCCTT CTCGCCCCAG GAGAAAGCCT GTAATCTTAA
1321  CTAGACCCAG CGCACCGGTA GCGAGAGGCC TCAGCAGCGC GGAGACCACC GACTCCGGTG
1381  CTTCCTCATC ACCCCCGGAG ATTCACCCCC TGGTGCCCCT ATGTCCCGTT AAGCCCGTTG
1441  CCGTGAGAGT CAGTGGGCGG CGGTCTGCTG TGGAGTGCAT TGAGGACTTG CTTTTTGATT
1501  CACAGGAACC TTTGGACTTG AGCTTGAAAC GCCCCAGGCA TTAAACCTGG TCACCTGGAC
1561  TGAATGAGTT GACGCCTATG TTTGCTTTTG AATGACTTAA TGTGTATAGA TAATAAAGAG
1621  TGAGATAATG TTTTAATTGC ATGGTGTGTT TAACTTGGGC GGAGTCTGCT GGGTATATAA
1681  GCTTCCCTGG GCTAAACTTG GTTACACTTG ACCTCATGGA GGCCTGGGAG TGTTTGGAGA
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Fig. 5A

SEQ ID NO:1


```
1741  ACTTTGCCGG AGTTCGTGCC TTGCTGGACG AGAGCTCTAA CAATACCTCT TGGTGGTGGA
1801  GGTATTTGTG GGGCTCTCCC CAGGGCAAGT TAGTTTGTAG AATCAAGGAG GATTACAAGT
1861  GGGAATTTGA AGAGCTTTTG AAATCCTGTG GTGAGCTATT GGATTCTTTG AATCTAGGCC
1921  ACCAGGCTCT CTTCCAGGAG AAGGTCATCA GGACTTTGGA TTTTTCCACA CCGGGGCGCA
1981  TTGCAGCCGC GGTTGCTTTT CTAGCTTTTT TGAAGGATAG ATGGAGCGAA GAGACCCACT
2041  TGAGTTCGGG CTACGTCCTG GATTTTCTGG CCATGCAACT GTGGAGAGCA TGGATCAGAC
2101  ACAAGAACAG GCTGCAACTG TTGTCTTCCG TCCGCCCGTT GCTGATTCCG GCGGAGGAGC
2161  AACAGGCCGG GTCAGAGGAC CGGGCCCGTC GGGATCCGGA GGAGAGGGCA CCGAGGCCGG
2221  GCGAGAGGAG CGCGCTGAAC CTGGGAACCG GGCTGAGCGG CCATCCACAT CGGGAGTGAA
2281  TGTCGGGCAG GTGGTGGATC TTTTTCCAGA ACTGCGGCGG ATTTTGACTA TTAGGGAGGA
2341  TGGGCAATTT GTTAAGGGTC TTAAGAGGGA GAGGGGGGCT TCTGAGCATA ACGAGGAGGC
2401  CAGTAATTTA GCTTTTAGCT TGATGACCAG ACACCGTCCA GAGTGCATCA CTTTTCAGCA
2461  GATTAAGGAC AATTGTGCCA ATGAGTTGGA TCTGTTGGGT CAGAAGTATA GCATAGAGCA
2521  GCTGACCACT TACTGGCTGC AGCCGGGTGA TGATCTGGAG GAAGCTATTA GGGTGTATGC
2581  TAAGGTGGCC CTGCGGCCCG ATTGCAAGTA CAAGCTCAAG GGGCTGGTGA ATATCAGGAA
2641  TTGTTGCTAC ATTTCTGGCA ACGGGGCGGA GGTGGAGATA GAGACCGAAG ACAGGGTGGC
2701  TTTCAGATGC AGCATGATGA ATATGTGGCC GGGGGTGCTG GGCATGGACG GGGTGGTGAT
2761  TATGAATGTG AGGTTCACGG GGCCCAACTT TAACGGCACG GTGTTTTTGG GGAACACCAA
2821  CCTGGTCCTG CACGGGGTGA GCTTCTATGG GTTTAACAAC ACCTGTGTGG AGGCCTGGAC
2881  CGATGTGAAG GTCCGCGGTT GCGCCTTTTA TGGATGTTGG AAGGCCATAG TGAGCCGCCC
2941  TAAGAGCAGG AGTTCCATTA AGAAATGCTT GTTTGAGAGG TGCACCTTGG GGATCCTGGC
3001  CGAGGGCAAC TGCAGGGTGC GCCACAATGT GGCCTCCGAG TGCGGTTGCT TCATGCTAGT
3061  CAAGAGCGTG GCGGTAATCA AGCATAATAT GGTGTGCGGC AACAGCGAGG ACAAGGCCTC
3121  ACAGATGCTG ACCTGCACGG ATGGCAACTG CCACTTGCTG AAGACCATCC ATGTAACCAG
3181  CCACAGCCGG AAGGCCTGGC CCGTGTTCGA GCACAACTTG CTGACCCGCT GCTCCTTGCA
3241  TCTGGGCAAC AGGCGGGGGG TGTTCCTGCC CTATCAATGC AACTTTAGTC ACACCAAGAT
3301  CTTGCTAGAG CCCGAGAGCA TGTCCAAGGT GAACTTGAAC GGGGTGTTTG ACATGACCAT
3361  GAAGATCTGG AAGGTGCTGA GGTACGACGA GACCAGGTCC CGGTGCAGAC CCTGCGAGTG
3421  CGGGGGCAAG CATATGAGGA ACCAGCCCGT GATGCTGGAT GTGACCGAGG AGCTGAGGAC
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Fig. 5B

SEQ ID NO:1


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3541  TTGAGGTGGG TGAGTGGGCG TGGCCTGGGG TGGTCATGAA AATATATAAG TTGGGGGTCT
3601  TAGGGTCTCT TTATTTGTGT TGCAGAGACC GCCGGAGCCA TGAGCGGGAG CAGCAGCAGC
3661  AGCAGTAGCA GCAGCGCCTT GGATGGCAGC ATCGTGAGCC CTTATTTGAC GACGCGGATG
3721  CCCCACTGGG CCGGGGTGCG TCAGAATGTG ATGGGCTCCA GCATCGACGG CCGACCCGTC
3781  CTGCCCGCAA ATTCCGCCAC GCTGACCTAT GCGACCGTCG CGGGGACGCC GTTGGACGCC
3841  ACCGCCGCCG CCGCCGCCAC CGCAGCCGCC TCGGCCGTGC GCAGCCTGGC CACGGACTTT
3901  GCATTCCTGG GACCACTGGC GACAGGGGCT ACTTCTCGGG CCGCTGCTGC CGCCGTTCGC
3961  GATGACAAGC TGACCGCCCT GCTGGCGCAG TTGGATGCGC TTACTCGGGA ACTGGGTGAC
4021  CTTTCTCAGC AGGTCATGGC CCTGCGCCAG CAGGTCTCCT CCCTGCAAGC TGGCGGGAAT
4081  GCTTCTCCCA CAAATGCCGT TTAAGATAAA TAAAACCAGA CTCTGTTTGG ATTAAAGAAA
4141  AGTAGCAAGT GCATTGCTCT CTTTATTTCA TAATTTTCCG CGCGCGATAG GCCCTAGACC
4201  AGCGTTCTCG GTCGTTGAGG GTGCGGTGTA TCTTCTCCAG GACGTGGTAG AGGTGGCTCT
4261  GGACGTTGAG ATACATGGGC ATGAGCCCGT CCCGGGGGTG GAGGTAGCAC CACTGCAGAG
4321  CTTCATGCTC CGGGGTGGTG TTGTAGATGA TCCAGTCGTA GCAGGAGCGC TGGGCATGGT
4381  GCCTAAAAAT GTCCTTCAGC AGCAGGCCGA TGGCCAGGGG GAGGCCCTTG GTGTAAGTGT
4441  TTACAAAACG GTTAAGTTGG GAAGGGTGCA TTCGGGGAGA GATGATGTGC ATCTTGGACT
4501  GTATTTTTAG ATTGGCGATG TTTCCGCCCA GATCCCTTCT GGGATTCATG TTGTGCAGGA
4561  CCACCAGTAC AGTGTATCCG GTGCACTTGG GGAATTTGTC ATGCAGCTTA GAGGGAAAAG
4621  CGTGGAAGAA CTTGGAGACG CCCTTGTGGC CTCCCAGATT TTCCATGCAT TCGTCCATGA
4681  TGATGGCAAT GGGCCCGCGG GAGGCAGCTT GGGCAAAGAT ATTTCTGGGG TCGCTGACGT
4741  CGTAGTTGTG TTCCAGGGTG AGGTCGTCAT AGGCCATTTT TACAAAGCGC GGGCGGAGGG
4801  TGCCCGACTG GGGGATGATG GTCCCCTCTG GCCCTGGGGC GTAGTTGCCC TCGCAGATCT
4861  GCATTTCCCA GGCCTTAATC TCGGAGGGGG GAATCATATC CACCTGCGGG GCGATGAAGA
4921  AAACGGTTTC CGGAGCCGGG GAGATTAACT GGGATGAGAG CAGGTTTCTA AGCAGCTGTG
4981  ATTTTCCACA ACCGGTGGGC CCATAAATAA CACCTATAAC CGGTTGCAGC TGGTAGTTTA
5041  GAGAGCTGCA GCTGCCGTCG TCCCGGAGGA GGGGGGCCAC CTCGTTGAGC ATGTCCCTGA
5101  CGCGCATGTT CTCCCCGACC AGATCCGCCA GAAGGCGCTC GCCGCCCAGG GACAGCAGCT
5161  CTTGCAAGGA AGCAAAGTTT TTCAGCGGCT TGAGGCCGTC CGCCGTGGGC ATGTTTTTCA
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Fig. 5C

SEQ ID NO:1


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5341  GTGGTCGTCC AGCGGGGCCA AAGTCATGTC CTTCCATGGG CGCAGGGTCC TCGTCAGGGT
5401  GGTCTGGGTC ACGGTGAAGG GGTGCGCTCC GGGCTGAGCG CTTGCCAAGG TGCGCTTGAG
5461  GCTGGTTCTG CTGGTGCTGA AGCGCTGCCG GTCTTCGCCC TGCGCGTCGG CCAGGTAGCA
5521  TTTGACCATG GTGTCATAGT CCAGCCCCTC CGCGGCGTGT CCCTTGGCGC GCAGCTTGCC
5581  CTTGGAGGTG GCGCCGCACG AGGGGCAGAG CAGGCTCTTG AGCGCGTAGA GCTTGGGGGC
5641  GAGGAAGACC GATTCGGGGG AGTAGGCGTC CGCGCCGCAG ACCCCGCACA CGGTCTCGCA
5701  CTCCACCAGC CAGGTGAGCT CGGGGCGCGC CGGGTCAAAA ACCAGGTTTC CCCCATGCTT
5761  TTTGATGCGT TTCTTACCTC GGGTCTCCAT GAGGTGGTGT CCCCGCTCGG TGACGAAGAG
5821  GCTGTCCGTG TCTCCGTAGA CCGACTTGAG GGGTCTTTTC TCCAGGGGGG TCCCTCGGTC
5881  TTCCTCGTAG AGGAACTCGG ACCACTCTGA GACGAAGGCC CGCGTCCAGG CCAGGACGAA
5941  GGAGGCTATG TGGGAGGGGT AGCGGTCGTT GTCCACTAGG GGGTCCACCT TCTCCAAGGT
6001  GTGAAGACAC ATGTCGCCTT CCTCGGCGTC CAGGAAGGTG ATTGGCTTGT AGGTGTAGGC
6061  CACGTGACCG GGGGTTCCTG ACGGGGGGGT ATAAAAGGGG GTGGGGGCGC GCTCGTCGTC
6121  ACTCTCTTCC GCATCGCTGT CTGCGAGGGC CAGCTGCTGG GGTGAGTATT CCCTCTCGAA
6181  GGCGGGCATG ACCTCCGCGC TGAGGTTGTC AGTTTCCAAA AACGAGGAGG ATTTGATGTT
6241  CACCTGTCCC GAGGTGATAC CTTTGAGGGT ACCCGCGTCC ATCTGGTCAG AAAACACGAT
6301  CTTTTTATTG TCCAGCTTGG TGGCGAACGA CCCGTAGAGG GCGTTGGAGA GCAGCTTGGC
6361  GATGGAGCGC AGGGTCTGGT TCTTGTCCCT GTCGGCGCGC TCCTTGGCCG CGATGTTGAG
6421  CTGCACGTAC TCGCGCGCGA CGCAGCGCCA CTCGGGGAAG ACGGTGGTGC GCTCGTCGGG
6481  CACCAGGCGC ACGCGCCAGC CGCGGTTGTG CAGGGTGACC AGGTCCACGC TGGTGGCGAC
6541  CTCGCCGCGC AGGCGCTCGT TGGTCCAGCA GAGACGGCCG CCCTTGCGCG AGCAGAAGGG
6601  GGGCAGGGGG TCGAGCTGGG TCTCGTCCGG GGGGTCCGCG TCCACGGTGA AAACCCCGGG
6661  GCGCAGGCGC GCGTCGAAGT AGTCTATCTT GCAACCTTGC ATGTCCAGCG CCTGCTGCCA
6721  GTCGCGGGCG GCGAGCGCGC GCTCGTAGGG GTTGAGCGGC GGGCCCCAGG GCATGGGGTG
6781  GGTGAGTGCG GAGGCGTACA TGCCGCAGAT GTCATAGACG TAGAGGGGCT CCCGCAGGAC
6841  CCCGATGTAG GTGGGGTAGC AGCGGCCGCC GCGGATGCTG GCGCGCACGT AGTCATACAG
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Fig. 5D

SEQ ID NO:1

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7081 CAGCTTGTGT ACCAGCTCGG CGGTGACCTG CACGTCGAGC GCGCAGTAGT CGAGGGTCTC

7141 GCGGATGATG TCATATTTAG CCTGCCCCTT CTTTTTCCAC AGCTCGCGGT TGAGGACAAA

7201 CTCTTCGCGG TCTTTCCAGT ACTCTTGGAT CGGGAAACCG TCCGGTTCCG AACGGTAAGA

7261 GCCTAGCATG TAGAACTGGT TGACGGCCTG GTAGGCGCAG CAGCCCTTCT CCACGGGGAG

7321 GGCGTAGGCC TGCGCGGCCT TGCGGAGCGA GGTGTGGGTC AGGGCGAAGG TGTCCCTGAC

7381 CATGACTTTG AGGTACTGGT GCTTGAAGTC GGAGTCGTCG CAGCCGCCCC GCTCCCAGAG

7441 CGAGAAGTCG GTGCGCTTCT TGGAGCGGGG GTTGGGCAGA GCGAAGGTGA CATCGTTGAA

7501 GAGGATTTTG CCCGCGCGGG GCATGAAGTT GCGGGTGATG CGGAAGGGCC CCGGCACTTC

7561 AGAGCGGTTG TTGATGACCT GGGCGGCGAG CACGATCTCG TCGAAGCCGT TGATGTTGTG

7621 GCCCACGATG TAGAGTTCCA GGAAGCGGGG CCGGCCCTTT ACGGTGGGCA GCTTCTTTAG

7681 CTCTTCGTAG GTGAGCTCCT CGGGCGAGGC GAGGCCGTGC TCGGCCAGGG CCCAGTCCGC

7741 GAGGTGCGGG TTGTCTCTGA GGAAGGACTC CCAGAGGTCG CGGGCCAGGA GGGTCTGCAG

7801 GCGGTCCCTG AAGGTCCTGA ACTGGCGGCC CACGGCCATT TTTTCGGGGG TGATGCAGTA

7861 GAAGGTGAGG GGGTCTTGCT GCCAGCGGTC CCAGTCGAGC TGCAGGGCGA GGTCGCGCGC

7921 GGCGGTGACC AGGCGCTCGT CGCCCCCGAA TTTCATGACC AGCATGAAGG GCACGAGCTG

7981 CTTTCCGAAG GCCCCCATCC AAGTGTAGGT CTCTACATCG TAGGTGACAA AGAGGCGCTC

8041 CGTGCGAGGA TGCGAGCCGA TCGGGAAGAA CTGGATCTCC CGCCACCAGT TGGAGGAGTG

8101 GCTGTTGATG TGGTGGAAGT AGAAGTCCCG TCGCCGGGCC GAACACTCGT GCTGGCTTTT

8161 GTAAAAGCGA GCGCAGTACT GGCAGCGCTG CACGGGCTGT ACCTCCTGCA CGAGATGCAC

8221 CTTTCGCCCG CGCACGAGGA AGCCGAGGGG AAATCTGAGC CCCCCGCCTG GCTCGCGGCA

8281 TGGCTGGTGC TCTTCTACTT TGGATGCGTG TCCGTCTCCG TCTGGCTCCT CGAGGGGTGT

8341 TACGGTGGAG CGGACCACCA CGCCGCGCGA GCCGCAGGTC CAGATATCGG CGCGCGGCGG

8401 TCGGAGTTTG ATGACGACAT CGCGCAGCTG GGAGCTGTCC ATGGTCTGGA GCTCCCGCGG

8461 CGGCGGCAGG TCAGCCGGGA GTTCTTGCAG GTTCACCTCG CAGAGTCGGG CCAGGGCGCG

8521 GGGCAGGTCT AGGTGGTACC TGATCTCTAG GGGCGTGTTG GTGGCGGCGT CGATGGCTTG

8581 CAGGAGCCCG CATCCCCGGG GGGCGACGAC GGTGCCCCGC GGGGTGGTGG TGGTGGTGGT

8641 GGTGGTGGTG GTGGCGGTGC AGCTCAGAAG CGGTGCCGCG GGCGGGCCCC CGGAGGTAGG

Fig. 5E

SEQ ID NO:1


```
 8701  GGGGGCTCCG GTCCCGCCGG CAGGGGCGGC AGCGGCACGT CGGCGTGGAG CGCGGGCAGG
 8761  AGTTGGTGCT GTGCCCGGAG GTTGCTGGCG AAGGCGACGA CGCGGCGGTT GATCTCCTGG
 8821  ATCTGGCGCC TCTGCGTGAA GACGACGGGC CCGGTGAGCT TGAACCTGAA AGAGAGTTCG
 8881  ACAGAATCAA TCTCGGTGTC ATTGACCGCG GCCTGGCGCA GGATCTCCTG CACGTCTCCC
 8941  GAGTTGTCTT GGTAGGCGAT CTCGGCCATG AACTGCTCGA TCTCTTCCTC CTGGAGGTCT
 9001  CCGCGTCCGG CGCGTTCCAC GGTGGCCGCC AGGTCGTTGG AGATGCGCCC CATGAGCTGC
 9061  GAGAAGGCGT TGAGTCCGCC CTCGTTCCAG ACTCGGCTGT AGACCACGCC CCCCTGGTCA
 9121  TCGCGGGCGC GCATGACCAC CTGCGCGAGG TTGAGCTCCA CGTGCCGCGC GAAGACGGCG
 9181  TAGTTGCGCA GACGCTGGAA GAGGTAGTTG AGGGTGGTGG CGGTGTGCTC GGCCACGAAG
 9241  AAGTTCATGA CCCAGCGGCG CAACGTGGAT TCGTTGATGT CCCCCAAGGC CTCCAGCCGT
 9301  TCCATGGCCT CGTAGAAGTC CACGGCGAAG TTGAAAAACT GGGAGTTGCG CGCCGACACG
 9361  GTCAACTCCT CCTCCAGAAG ACGGATGAGC TCGGCGACGG TGTCGCGCAC CTCGCGCTCG
 9421  AAGGCTATGG GGATCTCTTC CTCCGCTAGC ATCACCACCT CCTCCTCTTC CTCCTCTTCT
 9481  GGCACTTCCA TGATGGCTTC CTCCTCTTCG GGGGGCGGCG GCGGCGGCGG TGGGGGAGGG
 9541  GGCGCTCTGC GCCGGCGGCG GCGCACCGGG AGGCGGTCCA CGAAGCGCGC GATCATCTCC
 9601  CCGCGGCGGC GGCGCATGGT CTCGGTGACG GCGCGGCCGT TCTCCCGGGG GCGCAGTTGG
 9661  AAGACGCCGC CGGACATCTG GTGCTGGGGC GGGTGGCCGT GAGGCAGCGA AACGGCGCTG
 9721  ACGATGCATC TCAACAATTG CTGCGTAGGT ACGCCGCCGA GGGACCTGAG GGAGTCCATA
 9781  TCCACCGGAT CCGAAAACCT TTCGAGGAAG GCGTCTAACC AGTCGCAGTC GCAAGGTAGG
 9841  CTGAGCACCG TGGCGGGCGG CGGGGGGTGG GGGGAGTGTC TGGCGGAGGT GCTGCTGATG
 9901  ATGTAATTGA AGTAGGCGGA CTTGACACGG CGGATGGTCG ACAGGAGCAC CATGTCCTTG
 9961  GGTCCGGCCT GCTGGATGCG GAGGCGGTCG GCTATGCCCC AGGCTTCGTT CTGGCATCGG
10021  CGCAGGTCCT TGTAGTAGTC TTGCATGAGC CTTTCCACCG GCACCTCTTC TCCTTCCTCT
10081  TCTGCTTCTT CCATGTCTGC TTCGGCCCTG GGGCGGCGCC GCGCCCCCCT GCCCCCCATG
10141  CGCGTGACCC CGAACCCCCT GAGCGGTTGG AGCAGGGCCA GGTCGGCGAC GACGCGCTCG
10201  GCCAGGATGG CCTGCTGCAC CTGCGTGAGG GTGGTTTGGA AGTCATCCAA GTCCACGAAG
10261  CGGTGGTAGG CGCCCGTGTT GATGGTGTAG GTGCAGTTGG CCATGACGGA CCAGTTGACG
10321  GTCTGGTGGC CCGGTTGCGA CATCTCGGTG TACCTGAGTC GCGAGTAGGC GCGGGAGTCG
10381  AAGACGTAGT CGTTGCAAGT CCGCACCAGG TACTGGTAGC CCACCAGGAA GTGCGGCGGC
```

Fig. 5F

SEQ ID NO:1


```
10441  GGCTGGCGGT AGAGGGGCCA GCGCAGGGTG GCGGGGGCTC CGGGGGCCAG GTCTTCCAGC
10501  ATGAGGCGGT GGTAGGCGTA GATGTACCTG GACATCCAGG TGATACCCGC GGCGGTGGTG
10561  GAGGCGCGCG GGAAGTCGCG CACCCGGTTC CAGATGTTGC GCAGGGGCAG AAAGTGCTCC
10621  ATGGTAGGCG TGCTCTGTCC AGTCAGACGC GCGCAGTCGT TGATACTCTA GACCAGGGAA
10681  AACGAAAGCC GGTCAGCGGG CACTCTTCCG TGGTCTGGTG AATAGATCGC AAGGGTATCA
10741  TGGCGGAGGG CCTCGGTTCG AGCCCCGGGT CCGGGCCGGA CGGTCCGCCA TGATCCACGC
10801  GGTTACCGCC CGCGTGTCGA ACCCAGGTGT GCGACGTCAG ACAACGGTGG AGTGTTCCTT
10861  TTGGCGTTTT TCTGGCCGGG CGCCGGCGTC GCGTAAGAGA CTAAGCCGCG AAAGCGAAAG
10921  CAGTAAGTGG CTCGCTCCCC GTAGCCGGAG GGATCCTTGC TAAGGGTTGC GTTGCGGCGA
10981  ACCCCGGTTC GAATCCCGTA CTCGGGCCGG CCGGACCCGC GGCTAAGGTG TTGGATTGGC
11041  CTCCCCCTCG TATAAAGACC CCGCTTGCGG ATTGACTCCG GACACGGGGA CGAGCCCCTT
11101  TTATTTTTGC TTTCCCCAGA TGCATCCGGT GCTGCGGCAG ATGCGCCCCC CGCCCCAGCA
11161  GCAGCAACAA CACCAGCAAG AGCGGCAGCA ACAGCAGCGG GAGTCATGCA GGGCCCCCTC
11221  ACCCACCCTC GGCGGGCCGG CCACCTCGGC GTCCGCGGCC GTGTCTGGCG CCTGCGGCGG
11281  CGGCGGGGGG CCGGCTGACG ACCCCGAGGA GCCCCCGCGG CGCAGGGCCA GACACTACCT
11341  GGACCTGGAG GAGGGCGAGG GCCTGGCGCG GCTGGGGGCG CCGTCTCCCG AGCGCCACCC
11401  GCGGGTGCAG CTGAAGCGCG ACTCGCGCGA GGCGTACGTG CCTCGGCAGA ACCTGTTCAG
11461  GGACCGCGCG GGCGAGGAGC CCGAGGAGAT GCGGGACAGG AGGTTCAGCG CAGGGCGGGA
11521  GCTGCGGCAG GGGCTGAACC GCGAGCGGCT GCTGCGCGAG GAGGACTTTG AGCCCGACGC
11581  GCGGACGGGG ATCAGCCCCG CGCGCGCGCA CGTGGCGGCC GCCGACCTGG TGACGGCGTA
11641  CGAGCAGACG GTGAACCAGG AGATCAACTT CCAAAAGAGT TTCAACAACC ACGTGCGCAC
11701  GCTGGTGGCG CGCGAGGAGG TGACCATCGG GCTGATGCAC CTGTGGGACT TTGTAAGCGC
11761  GCTGGTGCAG AACCCCAACA GCAAGCCTCT GACGGCGCAG CTGTTCCTGA TAGTGCAGCA
11821  CAGCAGGGAC AACGAGGCGT TTAGGGACGC GCTGCTGAAC ATCACCGAGC CCGAGGGTCG
11881  GTGGCTGCTG GACCTGATTA ACATCCTGCA GAGCATAGTG GTGCAGGAGC GCAGCCTGAG
11941  CCTGGCCGAC AAGGTGGCGG CCATCAACTA CTCGATGCTG AGCCTGGGCA AGTTTTACGC
12001  GCGCAAGATC TACCAGACGC CGTACGTGCC CATAGACAAG GAGGTGAAGA TCGACGGTTT
12061  TTACATGCGC ATGGCGCTGA AGGTGCTCAC CCTGAGCGAC GACCTGGGCG TGTACCGCAA
12121  CGAGCGCATC CACAAGGCCG TGAGCGTGAG CCGGCGGCGC GAGCTGAGCG ACCGCGAGCT
```

Fig. 5G

SEQ ID NO:1


```
12181  GATGCACAGC CTGCAGCGGG CGCTGGCGGG CGCCGGCAGC GGCGACAGGG AGGCGGAGTC
12241  CTACTTCGAT GCGGGGGCGG ACCTGCGCTG GGCGCCCAGC CGGCGGGCCC TGGAGGCCGC
12301  GGGGGTCCGC GAGGACTATG ACGAGGACGG CGAGGAGGAT GAGGAGTACG AGCTAGAGGA
12361  GGGCGAGTAC CTGGACTAAA CCGCGGGTGG TGTTTCCGGT AGATGCAAGA CCCGAACGTG
12421  GTGGACCCGG CGCTGCGGGC GGCTCTGCAG AGCCAGCCGT CCGGCCTTAA CTCCTCAGAC
12481  GACTGGCGAC AGGTCATGGA CCGCATCATG TCGCTGACGG CGCGTAACCC GGACGCGTTC
12541  CGGCAGCAGC CGCAGGCCAA CAGGCTCTCC GCCATCCTGG AGGCGGTGGT GCCTGCGCGC
12601  TCGAACCCCA CGCACGAGAA GGTGCTGGCC ATAGTGAACG CGCTGGCCGA GAACAGGGCC
12661  ATCCGCCCGG ACGAGGCCGG GCTGGTGTAC GACGCGCTGC TGCAGCGCGT GGCCCGCTAC
12721  AACAGCGGCA ACGTGCAGAC CAACCTGGAC CGGCTGGTGG GGGACGTGCG CGAGGCGGTG
12781  GCGCAGCGCG AGCGCGCGGA TCGGCAGGGC AACCTGGGCT CCATGGTGGC GCTGAATGCC
12841  TTCCTGAGCA CGCAGCCGGC CAACGTGCCG CGGGGGCAGG AAGACTACAC CAACTTTGTG
12901  AGCGCGCTGC GGCTGATGGT GACCGAGACC CCCCAGAGCG AGGTGTACCA GTCGGGCCCG
12961  GACTACTTCT TCCAGACCAG CAGACAGGGC CTGCAGACGG TGAACCTGAG CCAGGCTTTC
13021  AAGAACCTGC GGGGGCTGTG GGGCGTGAAG GCGCCCACCG GCGACCGGGC GACGGTGTCC
13081  AGCCTGCTGA CGCCCAACTC GCGCCTGCTG CTGCTGCTGA TCGCGCCGTT CACGGACAGC
13141  GGCAGCGTGT CCCGGGACAC CTACCTGGGG CACCTGCTGA CCCTGTACCG CGAGGCCATC
13201  GGGCAGGCGC AGGTGGACGA GCACACCTTC CAGGAGATCA CCAGCGTGAG CCGCGCGCTG
13261  GGGCAGGAGG ACACGAGCAG CCTGGAGGCG ACTCTGAACT ACCTGCTGAC CAACCGGCGG
13321  CAGAAGATTC CCTCGCTGCA CAGCCTGACC TCCGAGGAGG AGCGCATCTT GCGCTACGTG
13381  CAGCAGAGCG TGAGCCTGAA CCTGATGCGC GACGGGGTGA CGCCCAGCGT GGCGCTGGAC
13441  ATGACCGCGC GCAACATGGA ACCGGGCATG TACGCCGCGC ACCGGCCTTA CATCAACCGC
13501  CTGATGGACT ACCTGCATCG CGCGGCGGCC GTGAACCCCG AGTACTTTAC CAACGCCATC
13561  CTGAACCCGC ACTGGCTCCC GCCGCCCGGG TTCTACAGCG GGGGCTTCGA GGTCCCGGAG
13621  GCCAACGATG GCTTCCTGTG GGACGACATG GACGACAGCG TGTTCTCCCC GCGGCCGCAG
13681  GCGCTGGCGG AAGCGTCCCT GCTGCGTCCC AAGAAGGAGG AGGAGGAGGC GAGTCGCCGC
13741  CGCGGCAGCA GCGGCGTGGC TTCTCTGTCC GAGCTGGGGG CGGCAGCCGC CGCGCGCCCC
13801  GGGTCCCTGG GCGGCAGCCC CTTTCCGAGC CTGGTGGGGT CTCTGCACAG CGAGCGCACC
13861  ACCCGCCCTC GGCTGCTGGG CGAGGACGAG TACCTGAATA ACTCCCTGCT GCAGCCGGTG
```

Fig. 5H

SEQ ID NO:1


```
13921  CGGGAGAAAA ACCTGCCCCC CGCCTTCCCC AACAACGGGA TAGAGAGCCT GGTGGACAAG
13981  ATGAGCAGAT GGAAGACCTA TGCGCAGGAG CACAGGGACG CGCCCGCGCT CCGGCCGCCC
14041  ACGCGGCGCC AGCGCCACGA CCGGCAGCGG GGGCTGGTGT GGGATGACGA GGACTCCGCG
14101  GACGATAGCA GCGTGCTGGA CCTGGGAGGG AGCGGCAACC CGTTCGCGCA CCTGCGCCCC
14161  CGCCTGGGGA GGATGTTTTA AAAAAAAAAA AAGCAAGAAG CATGATGCAA AATTAAATAA
14221  AACTCACCAA GGCCATGGCG ACCGAGCGTT GGTTTCTTGT GTTCCCTTCA GTATGCGGCG
14281  CGCGGCGATG TACCAGGAGG GACCTCCTCC CTCTTACGAG AGCGTGGTGG GCGCGGCGGC
14341  GGCGGCGCCC TCTTCTCCCT TTGCGTCGCA GCTGCTGGAG CCGCCGTACG TGCCTCCGCG
14401  CTACCTGCGG CCTACGGGGG GGAGAAACAG CATCCGTTAC TCGGAGCTGG CGCCCCTGTT
14461  CGACACCACC CGGGTGTACC TGGTGGACAA CAAGTCGGCG GACGTGGCCT CCCTGAACTA
14521  CCAGAACGAC CACAGCAATT TTTTGACCAC GGTCATCCAG AACAATGACT ACAGCCCGAG
14581  CGAGGCCAGC ACCCAGACCA TCAATCTGGA TGACCGGTCG CACTGGGGCG GCGACCTGAA
14641  AACCATCCTG CACACCAACA TGCCCAACGT GAACGAGTTC ATGTTCACCA ATAAGTTCAA
14701  GGCGCGGGTG ATGGTGTCGC GCTCGCACAC CAAGGAAGAC CGGGTGGAGC TGAAGTACGA
14761  GTGGGTGGAG TTCGAGCTGC CAGAGGGCAA CTACTCCGAG ACCATGACCA TTGACCTGAT
14821  GAACAACGCG ATCGTGGAGC ACTATCTGAA AGTGGGCAGG CAAAACGGGG TCCTGGAGAG
14881  CGACATCGGG GTCAAGTTCG ACACCAGGAA CTTCCGCCTG GGGCTGGACC CCGTGACCGG
14941  GCTGGTTATG CCCGGGGTGT ACACCAACGA GGCCTTCCAT CCCGACATCA TCCTGCTGCC
15001  CGGCTGCGGG GTGGACTTCA CTTACAGCCG CCTGAGCAAC CTCCTGGGCA TCCGCAAGCG
15061  GCAGCCCTTC CAGGAGGGCT TCAGGATCAC CTACGAGGAC CTGGAGGGGG GCAACATCCC
15121  CGCGCTCCTC GATGTGGAGG CCTACCAGGA TAGCTTGAAG GAAAATGAGG CGGGACAGGA
15181  GGATACCACC CCCGCCGCCT CCGCCGCCGC CGAGCAGGGC GAGGATGCTG CTGACACCGC
15241  GGCCGCGGAC GGGGCAGAGG CCGACCCCGC TATGGTGGTG GAGGCTCCCG AGCAGGAGGA
15301  GGATATGAAT GACAGTGCGG TGCGCGGAGA CACCTTCGTC ACCCGGGGGG AGGAAAAGCA
15361  AGCGGAGGCC GAGGCCGCGG CCGAGGAAAA GCAACTGGCG GCAGCAGCGG CGGCGGCGGC
15421  GTTGGCCGCG GCGGAGGCTG AGTCTGAGGG GACCAAGCCC GCCAAGGAGC CCGTGATTAA
15481  GCCCCTGACC GAAGATAGCA AGAAGCGCAG TTACAACCTG CTCAAGGACA GCACCAACAC
15541  CGCGTACCGC AGCTGGTACC TGGCCTACAA CTACGGCGAC CCGTCGACGG GGGTGCGCTC
15601  CTGGACCCTG CTGTGCACGC CGGACGTGAC CTGCGGCTCG GAGCAGGTGT ACTGGTCGCT
```

Fig. 5I

SEQ ID NO:1

15661 GCCCGACATG ATGCAAGACC CCGTGACCTT CCGCTCCACG CGGCAGGTCA GCAACTTCCC

15721 GGTGGTGGGC GCCGAGCTGC TGCCCGTGCA CTCCAAGAGC TTCTACAACG ACCAGGCCGT

15781 CTACTCCCAG CTCATCCGCC AGTTCACCTC TCTGACCCAC GTGTTCAATC GCTTTCCTGA

15841 GAACCAGATT CTGGCGCGCC CGCCCGCCCC CACCATCACC ACCGTCAGTG AAAACGTTCC

15901 TGCTCTCACA GATCACGGGA CGCTACCGCT GCGCAACAGC ATCGGAGGAG TCCAGCGAGT

15961 GACCGTTACT GACGCCAGAC GCCGCACCTG CCCCTACGTT TACAAGGCCT TGGGCATAGT

16021 CTCGCCGCGC GTCCTTTCCA GCCGCACTTT TTGAGCAACA CCACCATCAT GTCCATCCTG

16081 ATCTCACCCA GCAATAACTC CGGCTGGGGA CTGCTGCGCG CGCCCAGCAA GATGTTCGGA

16141 GGGGCGAGGA AGCGTTCCGA GCAGCACCCC GTGCGCGTGC GCGGGCACTT CCGCGCCCCC

16201 TGGGGAGCGC ACAAACGCGG CCGCGCGGGG CGCACCACCG TGGACGACGC CATCGACTCG

16261 GTGGTGGAGC AGGCGCGCAA CTACAGGCCC GCGGTCTCTA CCGTGGACGC GGCCATCCAG

16321 ACCGTGGTGC GGGGCGCGCG GCGGTACGCC AAGCTGAAGA GCCGCCGGAA GCGCGTGGCC

16381 CGCCGCCACC GCCGCCGACC CGGGGCCGCC GCCAAACGCG CCGCCGCGGC CCTGCTTCGC

16441 CGGGCCAAGC GCACGGGCCG CCGCGCCGCC ATGAGGGCCG CGCGCCGCTT GGCCGCCGGC

16501 ATCACCGCCG CCACCATGGC CCCCCGTACC CGAAGACGCG CGGCCGCCGC CGCCGCCGCC

16561 GCCATCAGTG ACATGGCCAG CAGGCGCCGG GGCAACGTGT ACTGGGTGCG CGACTCGGTG

16621 ACCGGCACGC GCGTGCCCGT GCGCTTCCGC CCCCCGCGGA CTTGAGATGA TGTGAAAAAA

16681 CAACACTGAG TCTCCTGCTG TTGTGTGTAT CCCAGCGGCG GCGGCGCGCG CAGCGTCATG

16741 TCCAAGCGCA AAATCAAAGA AGAGATGCTC CAGGTCGTCG CGCCGGAGAT CTATGGGCCC

16801 CCGAAGAAGG AAGAGCAGGA TTCGAAGCCC CGCAAGATAA AGCGGGTCAA AAAGAAAAAG

16861 AAAGATGATG ACGATGCCGA TGGGGAGGTG GAGTTCCTGC GCGCCACGGC GCCCAGGCGC

16921 CCGGTGCAGT GGAAGGGCCG GCGCGTAAAG CGCGTCCTGC GCCCCGGCAC CGCGGTGGTC

16981 TTCACGCCCG GCGAGCGCTC CACCCGGACT TTCAAGCGCG TCTATGACGA GGTGTACGGC

17041 GACGAAGACC TGCTGGAGCA GGCCAACGAG CGCTTCGGAG AGTTTGCTTA CGGGAAGCGT

17101 CAGCGGGCGC TGGGGAAGGA GGACCTGCTG GCGCTGCCGC TGGACCAGGG CAACCCCACC

17161 CCCAGTCTGA AGCCCGTGAC CCTGCAGCAG GTGCTGCCGA GCAGCGCACC CTCCGAGGCG

17221 AAGCGGGGTC TGAAGCGCGA GGGCGGCGAC CTGGCGCCCA CCGTGCAGCT CATGGTGCCC

17281 AAGCGGCAGA GGCTGGAGGA TGTGCTGGAG AAAATGAAAG TAGACCCCGG TCTGCAGCCG

17341 GACATCAGGG TCCGTCCCAT CAAGCAGGTG GCGCCGGGCC TCGGCGTGCA GACCGTGGAC

Fig. 5J

SEQ ID NO:1


```
17401  GTGGTCATCC CCACCGGCAA CTCCCCCGCC GCCACCACCA CTACCGCTGC CTCCACGGAC
17461  ATGGAGACAC AGACCGATCC CGCCGCAGCC GCAGCCGCCG CCGCAGCCGC GACCTCCTCG
17521  GCGGAGGTGC AGACGGACCC CTGGCTGCCG CCGGCGATGT CAGCTCCCCG CGCGCGCCGC
17581  GGACGCAGAA AGTACGGCGC CGCCAACGCG CTCCTGCCCG AGTACGCCTT GCATCCTTCC
17641  ATCGCGCCCA CCCCCGGCTA CCGAGGCTAT ACCTACCGCC CGCGAAGAGC CAAGGGTTCC
17701  ACCCGCCGTC CCCGCCGACG CGCCGCCGCC ACCACCCGCC GCCGCCGCCG CAGACGCCAG
17761  CCCGCACTGG CTCCAGTCTC CGTGAGGAGA GTGGCGCGCG ACGGACACAC CCTGGTGCTG
17821  CCCAGGGCGC GCTACCACCC CAGCATCGTT TAAAAGCCTG TTGTGGTTCT TGCAGATATG
17881  GCCCTCACTT GCCGCCTCCG TTTCCCGGTG CCGGGATACC GAGGAGGAAG ATCGCGCCGC
17941  AGGAGGGGTC TGGCCGGCCG CGGCCTGAGC GGAGGCAGCC GCCGCGCGCA CCGGCGGCGA
18001  CGCGCCACCA GCCGACGCAT GCGCGGCGGG GTGCTGCCCC TGTTAATCCC CCTGATCGCC
18061  GCGGCGATCG GCGCCGTGCC CGGGATCGCC TCCGTGGCCT TGCAAGCGTC CCAGAGGCAT
18121  TGACAGACTT GCAAACTTGC AAATATGGAA AAAAAAAAAA AACCCCAATA AAAAGTCTAG
18181  ACTCTCACGC TCGCTTGGTC CTGTGACTAT TTTGTAGAAT GGAAGACATC AACTTTGCGT
18241  CGCTGGCCCC GCGTCACGGC TCGCGCCCGT TCCTGGGACA CTGGAACGAT ATCGGCACCA
18301  GCAACATGAG CGGTGGCGCC TTCAGTTGGG GCTCTCTGTG GAGCGGCATT AAAAGTATCG
18361  GGTCTGCCGT TAAAAATTAC GGCTCCCGGG CCTGGAACAG CAGCACGGGC CAGATGTTGA
18421  GAGACAAGTT GAAAGAGCAG AACTTCCAGC AGAAGGTGGT GGAGGGCCTG GCCTCCGGCA
18481  TCAACGGGGT GGTGGACCTG GCCAACCAGG CCGTGCAGAA TAAAATCAAC AGCAGACTGG
18541  ACCCCCGGCC GCCGGTGGAG GAGGTGCCGC CGGCGCTGGA GACGGTGTCC CCCGATGGGC
18601  GTGGCGAGAA GCGCCCGCGG CCCGATAGGG AAGAGACCAC TCTGGTCACG CAGACCGATG
18661  AGCCGCCCCC GTATGAGGAG GCCCTAAAGC AAGGTCTGCC CACCACGCGG CCCATCGCGC
18721  CCATGGCCAC CGGGGTGGTG GGCCGCCACA CCCCCGCCAC GCTGGACTTG CCTCCGCCCG
18781  CCGATGTGCC GCAGCAGCAG AAGGCGGCAC AGCCGGGCCC GCCCGCGACC GCCTCCCGTT
18841  CCTCCGCCGG TCCTCTGCGC CGCGCGGCCA GCGGCCCCCG CGGGGGGGTC GCGAGGCACG
18901  GCAACTGGCA GAGCACGCTG AACAGCATCG TGGGTCTGGG GGTGCGGTCC GTGAAGCGCC
18961  GCCGATGCTA CTGAATAGCT TAGCTAACGT GTTGTATGTG TGTATGCGCC CTATGTCGCC
19021  GCCAGAGGAG CTGCTGAGTC GCCGCCGTTC GCGCGCCCAC CACCACCGCC ACTCCGCCCC
19081  TCAAGATGGC GACCCCATCG ATGATGCCGC AGTGGTCGTA CATGCACATC TCGGGCCAGG
```

Fig. 5K

SEQ ID NO:1


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19141  ACGCCTCGGA GTACCTGAGC CCCGGGCTGG TGCAGTTCGC CCGCGCCACC GAGAGCTACT
19201  TCAGCCTGAG TAACAAGTTT AGGAACCCCA CGGTGGCGCC CACGCACGAT GTGACCACCG
19261  ACCGGTCTCA GCGCCTGACG CTGCGGTTCA TTCCCGTGGA CCGCGAGGAC ACCGCGTACT
19321  CGTACAAGGC GCGGTTCACC CTGGCCGTGG GCGACAACCG CGTGCTGGAC ATGGCCTCCA
19381  CCTACTTTGA CATCCGCGGG GTGCTGGACC GGGGTCCCAC TTTCAAGCCC TACTCTGGCA
19441  CCGCCTACAA CTCCCTGGCC CCCAAGGGCG CTCCCAACTC CTGCGAGTGG GAGCAAGAGG
19501  AAACTCAGGC AGTTGAAGAA GCAGCAGAAG AGGAAGAAGA AGATGCTGAC GGTCAAGCTG
19561  AGGAAGAGCA AGCAGCTACC AAAAAGACTC ATGTATATGC TCAGGCTCCC CTTTCTGGCG
19621  AAAAAATTAG TAAAGATGGT CTGCAAATAG GAACGGACGC TACAGCTACA GAACAAAAAC
19681  CTATTTATGC AGACCCTACA TTCCAGCCCG AACCCCAAAT CGGGGAGTCC CAGTGGAATG
19741  AGGCAGATGC TACAGTCGCC GGCGGTAGAG TGCTAAAGAA ATCTACTCCC ATGAAACCAT
19801  GCTATGGTTC CTATGCAAGA CCCACAAATG CTAATGGAGG TCAGGGTGTA CTAACGGCAA
19861  ATGCCCAGGG ACAGCTAGAA TCTCAGGTTG AAATGCAATT CTTTTCAACT TCTGAAAACG
19921  CCCGTAACGA GGCTAACAAC ATTCAGCCCA AATTGGTGCT GTATAGTGAG GATGTGCACA
19981  TGGAGACCCC GGATACGCAC CTTTCTTACA AGCCCGCAAA AAGCGATGAC AATTCAAAAA
20041  TCATGCTGGG TCAGCAGTCC ATGCCCAACA GACCTAATTA CATCGGCTTC AGAGACAACT
20101  TTATCGGCCT CATGTATTAC AATAGCACTG GCAACATGGG AGTGCTTGCA GGTCAGGCCT
20161  CTCAGTTGAA TGCAGTGGTG GACTTGCAAG ACAGAAACAC AGAACTGTCC TACCAGCTCT
20221  TGCTTGATTC CATGGGTGAC AGAACCAGAT ACTTTTCCAT GTGGAATCAG GCAGTGGACA
20281  GTTATGACCC AGATGTTAGA ATTATTGAAA ATCATGGAAC TGAAGACGAG CTCCCCAACT
20341  ATTGTTTCCC TCTGGGTGGC ATAGGGGTAA CTGACACTTA CCAGGCTGTT AAAACCAACA
20401  ATGGCAATAA CGGGGGCCAG GTGACTTGGA CAAAAGATGA AACTTTTGCA GATCGCAATG
20461  AAATAGGGGT GGGAAACAAT TTCGCTATGG AGATCAACCT CAGTGCCAAC CTGTGGAGAA
20521  ACTTCCTGTA CTCCAACGTG GCGCTGTACC TACCAGACAA GCTTAAGTAC AACCCCTCCA
20581  ATGTGGACAT CTCTGACAAC CCCAACACCT ACGATTACAT GAACAAGCGA GTGGTGGCCC
20641  CGGGGCTGGT GGACTGCTAC ATCAACCTGG GCGCGCGCTG GTCGCTGGAC TACATGGACA
20701  ACGTCAACCC CTTCAACCAC CACCGCAATG CGGGCCTGCG CTACCGCTCC ATGCTCCTGG
20761  GCAACGGGCG CTACGTGCCC TTCCACATCC AGGTGCCCCA GAAGTTCTTT GCCATCAAGA
20821  ACCTCCTCCT CCTGCCGGGC TCCTACACCT ACGAGTGGAA CTTCAGGAAG GATGTCAACA
```

Fig. 5L

SEQ ID NO:1


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20881  TGGTCCTCCA GAGCTCTCTG GGTAACGATC TCAGGGTGGA CGGGGCCAGC ATCAAGTTCG
20941  AGAGCATCTG CCTCTACGCC ACCTTCTTCC CCATGGCCCA CAACACGGCC TCCACGCTCG
21001  AGGCCATGCT CAGGAACGAC ACCAACGACC AGTCCTTCAA TGACTACCTT TCCGCCGCCA
21061  ACATGCTCTA CCCCATACCC GCCAACGCCA CCAACGTCCC CATCTCCATC CCCTCGCGCA
21121  ACTGGGCGGC CTTCCGCGGC TGGGCCTTCA CCCGCCTCAA GACCAAGGAG ACCCCCTCCC
21181  TGGGCTCGGG ATTCGACCCC TACTACACCT ACTCGGGCTC TATTCCCTAC CTGGACGGCA
21241  CCTTCTACCT CAACCACACT TTCAAGAAGG TCTCGGTCAC CTTCGACTCC TCGGTCAGCT
21301  GGCCGGGCAA CGACCGTCTG CTCACCCCCA ACGAGTTCGA GATCAAGCGC TCGGTCGACG
21361  GGGAAGGCTA CAACGTGGCC CAGTGCAACA TGACCAAGGA CTGGTTCCTG GTCCAGATGC
21421  TGGCCAACTA CAACATCGGC TACCAGGGCT TCTACATCCC AGAGAGCTAC AAGGACAGGA
21481  TGTACTCCTT CTTCAGGAAC TTCCAGCCCA TGAGCCGGCA GGTGGTGGAC CAGACCAAGT
21541  ACAAGGACTA CCAGGAGGTG GGCATCATCC ACCAGCACAA CAACTCGGGC TTCGTGGGCT
21601  ACCTCGCCCC CACCATGCGC GAGGGACAGG CCTACCCCGC CAACTTCCCC TACCCGCTCA
21661  TAGGCAAGAC CGCGGTCGAC AGCATCACCC AGAAAAAGTT CCTCTGCGAC CGCACCCTCT
21721  GGCGCATCCC CTTCTCCAGC AACTTCATGT CCATGGGTGC GCTCTCGGAC CTGGGCCAGA
21781  ACTTGCTCTA CGCCAACTCC GCCCACGCCC TCGACATGAC CTTCGAGGTC GACCCCATGG
21841  ACGAGCCCAC CCTTCTCTAT GTTCTGTTCG AAGTCTTTGA CGTGGTCCGG GTCCACCAGC
21901  CGCACCGCGG CGTCATCGAG ACCGTGTACC TGCGTACGCC CTTCTCGGCC GGCAACGCCA
21961  CCACCTAAAG AAGCAAGCCG CAGTCATCGC CGCCTGCATG CCGTCGGGTT CCACCGAGCA
22021  AGAGCTCAGG GCCATCGTCA GAGACCTGGG ATGCGGGCCC TATTTTTTGG GCACCTTCGA
22081  CAAGCGCTTC CCTGGCTTTG TCTCCCCACA CAAGCTGGCC TGCGCCATCG TCAACACGGC
22141  CGGCCGCGAG ACCGGGGGCG TGCACTGGCT GGCCTTTGCC TGGAACCCGC GCTCCAAAAC
22201  ATGCTTCCTC TTTGACCCCT TCGGCTTTTC GGACCAGCGG CTCAAGCAAA TCTACGAGTT
22261  CGAGTACGAG GGCTTGCTGC GTCGCAGCGC CATCGCCTCC TCGCCCGACC GCTGCGTCAC
22321  CCTCGAAAAG TCCACCCAGA CCGTGCAGGG GCCCGACTCG GCCGCCTGCG GTCTCTTCTG
22381  CTGCATGTTT CTGCACGCCT TTGTGCACTG GCCTCAGAGT CCCATGGACC GCAACCCCAC
22441  CATGAACTTG CTGACGGGGG TGCCCAACTC CATGCTCCAA AGCCCCCAGG TCGAGCCCAC
22501  CCTGCGCCGC AACCAGGAGC AGCTCTACAG CTTCCTGGAG CGCCACTCGC CCTACTTCCG
22561  CCGCCACAGC GCACAGATCA GGAGGGCCAC CTCCTTCTGC CACTTGCAAG AGATGCAAGA
```

Fig. 5M

SEQ ID NO:1


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22621  AGGGTAATAA CGATGTACAC ACTTTTTTCT CAATAAATGG CATTTTTTTT TTATTTATAC
22681  AAGCTCTCTG GGGTATTCAT TTCCCACCAC CACCACCCGC CGTTGTCGCC ATCTGGCTCT
22741  ATTTAGAAAT CGAAAGGGTT CTGCCGGGAG TCGCCGTGCG CCACGGGCAG GGACACGTTG
22801  CGATACTGGT AGCGGGTGCC CCACTTGAAC TCGGGCACCA CCAGGCGAGG CAGCTCGGGG
22861  AAGTTTTCGC TCCACAGGCT GCGGGTCAGC ACCAGCGCGT TCATCAGGTC GGGCGCCGAG
22921  ATCTTGAAGT CGCAGTTGGG GCCGCCGCCC TGCGCGCGCG AGTTGCGGTA CACCGGGTTG
22981  CAGCACTGGA ACACCAACAG CGCCGGGTGC TTCACGCTGG CCAGCACGCT GCGGTCGGAG
23041  ATCAGCTCGG CGTCCAGGTC CTCCGCGTTG CTCAGCGCGA ACGGGGTCAT CTTGGGCACT
23101  TGCCGCCCCA GGAAGGGCGC GTGCCCCGGT TTCGAGTTGC AGTCGCAGCG CAGCGGGATC
23161  AGCAGGTGCC CGTGCCCGGA CTCGGCGTTG GGGTACAGCG CGCGCATGAA GGCCTGCATC
23221  TGGCGGAAGG CCATCTGGGC CTTGGCGCCC TCCGAGAAGA ACATGCCGCA GGACTTGCCC
23281  GAGAACTGGT TTGCGGGGCA GCTGGCGTCG TGCAGGCAGC AGCGCGCGTC GGTGTTGGCG
23341  ATCTGCACCA CGTTGCGCCC CCACCGGTTC TTCACGATCT TGGCCTTGGA CGATTGCTCC
23401  TTCAGCGCGC GCTGCCCGTT CTCGCTGGTC ACATCCATCT CGATCACATG TTCCTTGTTC
23461  ACCATGCTGC TGCCGTGCAG ACACTTCAGC TCGCCCTCCG TCTCGGTGCA GCGGTGCTGC
23521  CACAGCGCGC AGCCCGTGGG CTCGAAAGAC TTGTAGGTCA CCTCCGCGAA GGACTGCAGG
23581  TACCCCTGCA AAAAGCGGCC CATCATGGTC ACGAAGGTCT TGTTGCTGCT GAAGGTCAGC
23641  TGCAGCCCGC GGTGCTCCTC GTTCAGCCAG GTCTTGCACA CGGCCGCCAG CGCCTCCACC
23701  TGGTCGGGCA GCATCTTGAA GTTCACCTTC AGCTCATTCT CCACGTGGTA CTTGTCCATC
23761  AGCGTGCGCG CCGCCTCCAT GCCCTTCTCC CAGGCCGACA CCAGCGGCAG GCTCACGGGG
23821  TTCTTCACCA TCACCGTGGC CGCCGCCTCC GCCGCGCTTT CGCTTTCCGC CCCGCTGTTC
23881  TCTTCCTCTT CCTCCTCTTC CTCGCCGCCG CCCACTCGCA GCCCCCGCAC CACGGGGTCG
23941  TCTTCCTGCA GGCGCTGCAC CTTGCGCTTG CCGTTGCGCC CCTGCTTGAT GCGCACGGGC
24001  GGGTTGCTGA AGCCCACCAT CACCAGCGCG GCCTCTTCTT GCTCGTCCTC GCTGTCCAGA
24061  ATGACCTCCG GGGAGGGGGG GTTGGTCATC CTCAGTACCG AGGCACGCTT CTTTTTCTTC
24121  CTGGGGGCGT TCGCCAGCTC CGCGGCTGCG GCCGCTGCCG AGGTCGAAGG CCGAGGGCTG
24181  GGCGTGCGCG GCACCAGCGC GTCTTGCGAG CCGTCCTCGT CCTCCTCGGA CTCGAGACGG
24241  AGGCGGGCCC GCTTCTTCGG GGGCGCGCGG GGCGGCGGAG GCGGCGGCGG CGACGGAGAC
24301  GGGGACGAGA CATCGTCCAG GGTGGGTGGA CGGCGGGCCG CGCCGCGTCC GCGCTCGGGG
```

Fig. 5N

SEQ ID NO:1


```
24361  GTGGTTTCGC GCTGGTCCTC TTCCCGACTG GCCATCTCCC ACTGCTCCTT CTCCTATAGG
24421  CAGAAAGAGA TCATGGAGTC TCTCATGCGA GTCGAGAAGG AGGAGGACAG CCTAACCGCC
24481  CCCTCTGAGC CCTCCACCAC CGCCGCCACC ACCGCCAATG CCGCCGCGGA CGACGCGCCC
24541  ACCGAGACCA CCGCCAGTAC CACCCTCCCC AGCGACGCAC CCCCGCTCGA GAATGAAGTG
24601  CTGATCGAGC AGGACCCGGG TTTTGTGAGC GGAGAGGAGG ATGAGGTGGA TGAGAAGGAG
24661  AAGGAGGAGG TCGCCGCCTC AGTGCCAAAA GAGGATAAAA AGCAAGACCA GGACGACGCA
24721  GATAAGGATG AGACAGCAGT CGGGCGGGGG AACGGAAGCC ATGATGCTGA TGACGGCTAC
24781  CTAGACGTGG GAGACGACGT GCTGCTTAAG CACCTGCACC GCCAGTGCGT CATCGTCTGC
24841  GACGCGCTGC AGGAGCGCTG CGAAGTGCCC CTGGACGTGG CGGAGGTCAG CCGCGCCTAC
24901  GAGCGGCACC TCTTCGCGCC GCACGTGCCC CCCAAGCGCC GGGAGAACGG CACCTGCGAG
24961  CCCAACCCGC GTCTCAACTT CTACCCGGTC TTCGCGGTAC CCGAGGTGCT GGCCACCTAC
25021  CACATCTTCT TCCAAAACTG CAAGATCCCC CTCTCCTGCC GCGCTAACCG CACCCGCGCC
25081  GACAAAACCC TGACCCTGCG GCAGGGCGCC CACATACCTG ATATTGCCTC TCTGGAGGAA
25141  GTGCCCAAGA TCTTCGAGGG TCTCGGTCGC GACGAGAAAC GGGCGGCGAA CGCTCTGCAC
25201  GGAGACAGCG AAAACGAGAG TCACTCGGGG GTGCTGGTGG AGCTCGAGGG CGACAACGCG
25261  CGCCTGGCCG TACTCAAGCG CAGCATAGAG GTCACCCACT TTGCCTACCC GGCGCTCAAC
25321  CTGCCCCCCA AGGTCATGAG TGTGGTCATG GGCGAGCTCA TCATGCGCCG CGCTCAGCCC
25381  CTGGCCGCGG ATGCAAACTT GCAAGAGTCC TCCGAGGAAG GCCTGCCCGC GGTCAGCGAC
25441  GAGCAGCTAG CGCGCTGGCT GGAGACCCGC GACCCCGCGC AGCTGGAGGA GCGGCGCAAG
25501  CTCATGATGG CCGCGGTGCT GGTCACCGTG GAGCTCGAGT GTCTGCAGCG CTTCTTCGCG
25561  GACCCCGAGA TGCAGCGCAA GCTCGAGGAG ACCCTGCACT ACACCTTCCG CCAGGGCTAC
25621  GTGCGCCAGG CCTGCAAGAT CTCCAACGTG GAGCTCTGCA ACCTGGTCTC CTACCTGGGC
25681  ATCCTGCACG AGAACCGCCT CGGGCAGAAC GTCCTGCACT CCACCCTCAA AGGGGAGGCG
25741  CGCCGCGACT ACATCCGCGA CTGCGCCTAC CTCTTCCTCT GCTACACCTG GCAGACGGCC
25801  ATGGGGGTCT GGCAGCAGTG CCTGGAGGAG CGCAACCTCA AGGAGCTGGA AAAGCTACTC
25861  AAGCGCACCC TCAGGGACCT CTGGACGGGC TTCAACGAGC GCTCGGTGGC CGCCGCGCTG
25921  GCGGACATCA TCTTCCCCGA GCGCCTGCTC AAGACCCTGC AGCAGGGCCT GCCCGACTTC
25981  ACCAGCCAGA GCATGCTGCA GAACTTTAGG ACTTTCATCC TGGAGCGCTC GGGCATCCTG
26041  CCTGCCACTT GCTGCGCGCT GCCCAGCGAC TTCGTGCCCA TCAAGTACAG GGAGTGCCCG
```

Fig. 50

SEQ ID NO:1


```
26101  CCGCCGCTCT GGGGCCACTG CTACCTCTTC CAGCTGGCCA ACTACCTCGC CTACCACTCG
26161  GACCTCATGG AAGACGTGAG CGGCGAGGGC CTGCTCGAGT GCCACTGCCG CTGCAACCTC
26221  TGCACGCCCC ACCGCTCTCT AGTCTGCAAC CCGCAGCTGC TCAGCGAGAG TCAGATTATC
26281  GGTACCTTCG AGCTGCAGGG TCCCTCGCCT GACGAGAAGT CCGCGGCTCC GGGGCTGAAA
26341  CTCACTCCGG GGCTGTGGAC TTCCGCCTAC CTACGCAAAT TTGTACCTGA GGACTACCAC
26401  GCCCACGAGA TCAGGTTCTA CGAAGACCAA TCCCGCCCGC CCAAGGCGGA GCTCACCGCC
26461  TGCGTCATCA CCCAGGGGCA CATCCTGGGC CAATTGCAAG CCATCAACAA AGCCCGCCGA
26521  GAGTTCTTGC TGAAAAAGGG TCGGGGGGTG TACCTGGACC CCCAGTCCGG CGAGGAGCTA
26581  AACCCGCTAC CCCCGCCGCC GCCCCAGCAG CGGGACCTTG CTTCCCAGGA TGGCACCCAG
26641  AAAGAAGCAG CAGCCGCCGC CGCCGCAGCC ATACATGCTT CTGGAGGAAG AGGAGGAGGA
26701  CTGGGACAGT CAGGCAGAGG AGGTTTCGGA CGAGGAGCAG GAGGAGATGA TGGAAGACTG
26761  GGAGGAGGAC AGCAGCCTAG ACGAGGAAGC TTCAGAGGCC GAAGAGGTGG CAGACGCAAC
26821  ACCATCACCC TCGGTCGCAG CCCCCTCGCC GGGGCCCCTG AAATCCTCCG AACCCAGCAC
26881  CAGCGCTATA ACCTCCGCTC CTCCGGCGCC GGCGCCACCC GCCCGCAGAC CCAACCGTAG
26941  ATGGGACACC ACAGGAACCG GGGTCGGTAA GTCCAAGTGC CCGCCGCCGC CACCGCAGCA
27001  GCAGCAGCAG CGCCAGGGCT ACCGCTCGTG GCGCGGGCAC AAGAACGCCA TAGTCGCCTG
27061  CTTGCAAGAC TGCGGGGGCA ACATCTCTTT CGCCCGGCGC TTCCTGCTAT TCCACCACGG
27121  GGTCGCCTTT CCCCGCAATG TCCTGCATTA CTACCGTCAT CTCTACAGCC CCTACTGCAG
27181  CGGCGACCCA GAGGCGGCAG CGGCAGCCAC AGCGGCGACC ACCACCTAGG AAGATATCCT
27241  CCGCGGGCAA GACAGCGGCA GCAGCGGCCA GGAGACCCGC GGCAGCAGCG GCGGGAGCGG
27301  TGGGCGCACT GCGCCTCTCG CCCAACGAAC CCCTCTCGAC CCGGGAGCTC AGACACAGGA
27361  TCTTCCCCAC TTTGTATGCC ATCTTCCAAC AGAGCAGAGG CCAGGAGCAG GAGCTGAAAA
27421  TAAAAAACAG ATCTCTGCGC TCCCTCACCC GCAGCTGTCT GTATCACAAA AGCGAAGATC
27481  AGCTTCGGCG CACGCTGGAG GACGCGGAGG CACTCTTCAG CAAATACTGC GCGCTCACTC
27541  TTAAAGACTA GCTCCGCGCC CTTCTCGAAT TTAGGCGGGA GAAAACTACG TCATCGCCGG
27601  CCGCCGCCCA GCCCGCCCAG CCGAGATGAG CAAAGAGATT CCCACGCCAT ACATGTGGAG
27661  CTACCAGCCG CAGATGGGAC TCGCGGCGGG AGCGGCCCAG GACTACTCCA CCCGCATGAA
27721  CTACATGAGC GCGGGACCCC ACATGATCTC ACAGGTCAAC GGGATCCGCG CCCAGCGAAA
27781  CCAAATACTG CTGGAACAGG CGGCCATCAC CGCCACGCCC CGCCATAATC TCAACCCCCG
```

Fig. 5P

SEQ ID NO:1


```
27841  AAATTGGCCC GCCGCCCTCG TGTACCAGGA AACCCCCTCC GCCACCACCG TACTACTTCC
27901  GCGTGACGCC CAGGCCGAAG TCCAGATGAC TAACTCAGGG GCGCAGCTCG CGGGCGGCTT
27961  TCGTCACGGG GCGCGGCCGC TCCGACCAGG TATAAGACAC CTGATGATCA GAGGCCGAGG
28021  TATCCAGCTC AACGACGAGT CGGTGAGCTC TTCGCTCGGT CTCCGTCCGG ACGGAACTTT
28081  CCAGCTCGCC GGATCCGGCC GCTCTTCGTT CACGCCCCGC CAGGCGTACC TGACTCTGCA
28141  GACCTCGTCC TCGGAGCCCC GCTCCGGAGG CATCGGAACC CTCCAGTTCG TGGAGGAGTT
28201  CGTGCCCTCG GTCTACTTCA ACCCCTTCTC GGGACCTCCC GGACGCTACC CCGACCAGTT
28261  CATTCCGAAC TTTGACGCGG TGAAGGACTC GGCGGACGGC TACGACTGAA TGTCAGGTGC
28321  CGAGGCAGAG CAGCTTCGCC TGAGACACCT CGAGCACTGC CGCCGCCACA AGTGCTTCGC
28381  CCGCGGTTCC GGTGAGTTCT GCTACTTTCA GCTACCCGAG GAGCATACCG AGGGGCCGGC
28441  GCACGGCGTC CGCCTGACCA CCCAGGGCGA GGTTACCTGT TCCCTCATCC GGGAGTTCAC
28501  CCTCCGTCCC CTGCTAGTGG AGCGGGAGCG GGGTCCCTGT GTCCTAACTA TCGCCTGCAA
28561  CTGCCCTAAC CCTGGATTAC ATCAAGATCT TTGCTGTCAT CTCTGTGCTG AGTTTAATAA
28621  ACGCTGAGAT CAGAATCTAC TGGGGCTCCT GTCGCCATCC TGTGAACGCC ACCGTCTTCA
28681  CCCACCCCGA CCAGGCCCAG GCGAACCTCA CCTGCGGTCT GCATCGGAGG GCCAAGAAGT
28741  ACCTCACCTG GTACTTCAAC GGCACCCCCT TTGTGGTTTA CAACAGCTTC GACGGGGACG
28801  GAGTCTCCCT GAAAGACCAG CTCTCCGGTC TCAGCTACTC CATCCACAAG AACACCACCC
28861  TCCAACTCTT CCCTCCCTAC CTGCCGGGAA CCTACGAGTG CGTCACCGGC CGCTGCACCC
28921  ACCTCACCCG CCTGATCGTA AACCAGAGCT TTCCGGGAAC AGATAACTCC CTCTTCCCCA
28981  GAACAGGAGG TGAGCTCAGG AAACTCCCCG GGGACCAGGG CGGAGACGTA CCTTCGACCC
29041  TTGTGGGGTT AGGATTTTTT ATTACCGGGT TGCTGGCTCT TTTAATCAAA GCTTCCTTGA
29101  GATTTGTTCT TTCCTTCTAC GTGTATGAAC ACCTCAGCCT CCAATAACTC TACCCTTTCT
29161  TCGGAATCAG GTGACTTCTC TGAAATCGGG CTTGGTGTGC TGCTTACTCT GTTGATTTTT
29221  TTCCTTATCA TACTCAGCCT TCTGTGCCTC AGGCTCGCCG CCTGCTGCGC ACACATCTAT
29281  ATCTACTGCT GGTTGCTCAA GTGCAGGGGT CGCCACCCAA GATGAACAGG TACATGGTCC
29341  TATCGATCCT AGGCCTGCTG GCCCTGGCGG CCTGCAGCGC CGCCAAAAAA GAGATTACCT
29401  TTGAGGAGCC CGCTTGCAAT GTAACTTTCA AGCCCGAGGG TGACCAATGC ACCACCCTCG
29461  TCAAATGCGT TACCAATCAT GAGAGGCTGC GCATCGACTA CAAAAACAAA ACTGGCCAGT
29521  TTGCGGTCTA TAGTGTGTTT ACGCCCGGAG ACCCCTCTAA CTACTCTGTC ACCGTCTTCC
```

Fig. 5Q

SEQ ID NO:1


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29581  AGGGCGGACA GTCTAAGATA TTCAATTACA CTTTCCCTTT TTATGAGTTA TGCGATGCGG
29641  TCATGTACAT GTCAAAACAG TACAACCTGT GGCCTCCCTC TCCCCAGGCG TGTGTGGAAA
29701  ATACTGGGTC TTACTGCTGT ATGGCTTTGG CAATCACTAC GCTCGCTCTA ATCTGCACGG
29761  TGCTATACAT AAAATTCAGG CAGAGGCGAA TCTTTATCGA TGAAAAGAAA ATGCCTTGAT
29821  CGCTAACACC GGCTTTCTAT CTGCAGAATG AATGCAATCA CCTCCCTACT AATCACCACC
29881  ACCCTCCTTG CGATTGCCCA TGGGTTGACA CGAATCGAAG TGCCAGTGGG GTCCAATGTC
29941  ACCATGGTGG GCCCCGCCGG CAATTCCACC CTCATGTGGG AAAAATTTGT CCGCAATCAA
30001  TGGGTTCATT TCTGCTCTAA CCGAATCAGT ATCAAGCCCA GAGCCATCTG CGATGGGCAA
30061  AATCTAACTC TGATCAATGT GCAAATGATG GATGCTGGGT ACTATTACGG GCAGCGGGGA
30121  GAAATCATTA ATTACTGGCG ACCCCACAAG GACTACATGC TGCATGTAGT CGAGGCACTT
30181  CCCACTACCA CCCCCACTAC CACCTCTCCC ACCACCACTA CCACCACTAC TACTACTACT
30241  ACTACCACTA CCGCTGCCCG CCATACCCGC AAAAGCACCA TGATTAGCAC AAAGCCCCCT
30301  CGTGCTCACT CCCACGCCGG CGGGCCCATC GGTGCGACCT CAGAAACCAC CGAGCTTTGC
30361  TTCTGCCAAT GCACTAACGC CAGCGCTCAT GAACTGTTCG ACCTGGAGAA TGAGGATGCC
30421  CAGCAGAGCT CCGCTTGCCT GACCCAGGAG GCTGTGGAGC CCGTTGCCCT GAAGCAGATC
30481  GGTGATTCAA TAATTGACTC TTCTTCTTTT GCCACTCCCG AATACCCTCC CGATTCTACT
30541  TTCCACATCA CGGGTACCAA AGACCCTAAC CTCTCTTTCT ACCTGATGCT GCTGCTCTGT
30601  ATCTCTGTGG TCTCTTCCGC GCTGATGTTA CTGGGGATGT TCTGCTGCCT GATCTGCCGC
30661  AGAAAGAGAA AAGCTCGCTC TCAGGGCCAA CCACTGATGC CCTTCCCCTA CCCCCCGGAT
30721  TTTGCAGATA ACAAGATATG AGCTCGCTGC TGACACTAAC CGCTTTACTA GCCTGCGCTC
30781  TAACCCTTGT CGCTTGCGAC TCGAGATTCC ACAATGTCAC AGCTGTGGCA GGAGAAAATG
30841  TTACTTTCAA CTCCACGGCC GATACCCAGT GGTCGTGGAG TGGCTCAGGT AGCTACTTAA
30901  CTATCTGCAA TAGCTCCACT TCCCCCAGCA TATCCCCAAC CAAGTACCAA TGCAATGCCA
30961  GCCTGTTCAC CCTCATCAAC GCTTCCACCC TGGACAATGG ACTCTATGTA GGCTATGTAC
31021  CCTTTGGTGG GCAAGGAAAG ACCCACGCTT ACAACCTGGA AGTTCGCCAG CCCAGAACCA
31081  CTACCCAAGC TTCTCCCACC ACCACCACCA CCACCACCAC CACCATCACC AGCAGCAGCA
31141  GCAGCCACAG CAGCAGCAGC AGATTATTGA CTTTGGTTTT GGCCAGCTCA TCTGCCGCTA
31201  CCCAGGCCAT CTACAGCTCT GTGCCCGAAA CCACTCAGAT CCACCGCCCA GAAACGACCA
31261  CCGCCACCAC CCTACACACC TCCAGCGATC AGATGCCGAC CAACATCACC CCCTTGGCTC
```

Fig. 5R

SEQ ID NO:1


```
31321  TTCAAATGGG ACTTACAAGC CCCACTCCAA AACCAGTGGA TGCGGCCGAG GTCTCCGCCC
31381  TCGTCAATGA CTGGGCGGGG CTGGGAATGT GGTGGTTCGC CATAGGCATG ATGGCGCTCT
31441  GCCTGCTTCT GCTCTGGCTC ATCTGCTGCC TCCACCGCAG GCGAGCCAGA CCCCCCATCT
31501  ATAGACCCAT CATTGTCCTG AACCCCGATA ATGATGGGAT CCATAGATTG GATGGCCTGA
31561  AAAACCTACT TTTTTCTTTT ACAGTATGAT AAATTGAGAC ATGCCTCGCA TTTTCTTGTA
31621  CATGTTCCTT CTCCCACCTT TTCTGGGGTG TTCTACGCTG GCCGCTGTGT CTCACCTGGA
31681  GGTAGACTGC CTCTCACCCT TCACTGTCTA CCTGCTTTAC GGATTGGTCA CCCTCACTCT
31741  CATCTGCAGC CTAATCACAG TAATCATCGC CTTCATCCAG TGCATTGATT ACATCTGTGT
31801  GCGCCTCGCA TACTTCAGAC ACCACCCGCA GTACCGAGAC AGGAACATTG CCCAACTTCT
31861  AAGACTGCTC TAATCATGCA TAAGACTGTG ATCTGCCTTC TGATCCTCTG CATCCTGCCC
31921  ACCCTCACCT CCTGCCAGTA CACCACAAAA TCTCCGCGCA AAAGACATGC CTCCTGCCGC
31981  TTCACCCAAC TGTGGAATAT ACCCAAATGC TACAACGAAA AGAGCGAGCT CTCCGAAGCT
32041  TGGCTGTATG GGGTCATCTG TGTCTTAGTT TTCTGCAGCA CTGTCTTTGC CCTCATGATC
32101  TACCCCTACT TTGATTTGGG ATGGAACGCG ATCGATGCCA TGAATTACCC CACCTTTCCC
32161  GCACCCGAGA TAATTCCACT GCGACAAGTT GTACCCGTTG TCGTTAATCA ACGCCCCCCA
32221  TCCCCTACGC CCACTGAAAT CAGCTACTTT AACCTAACAG GCGGAGATGA CTGACGCCCT
32281  AGATCTAGAA ATGGACGGCA TCAGTACCGA GCAGCGTCTC CTAGAGAGGC GCAGGCAGGC
32341  GGCTGAGCAA GAGCGCCTCA ATCAGGAGCT CCGAGATCTC GTTAACCTGC ACCAGTGCAA
32401  AAGAGGCATC TTTTGTCTGG TAAAGCAGGC CAAAGTCACC TACGAGAAGA CCGGCAACAG
32461  CCACCGCCTC AGTTACAAAT TGCCCACCCA GCGCCAGAAG CTGGTGCTCA TGGTGGGTGA
32521  GAATCCCATC ACCGTCACCC AGCACTCGGT AGAGACCGAG GGGTGTCTGC ACTCTCCCTG
32581  TCGGGGTCCA GAAGACCTCT GCACCCTGGT AAAGACCCTG TGCGGTCTCA GAGATTTAGT
32641  CCCCTTTAAC TAATCAAACA CTGGAATCAA TAAAAAGAAT CACTTACTTA AAATCAGACA
32701  GCAGGTCTCT GTCCAGTTTA TTCAGCAGCA CCTCCTTCCC CTCCTCCCAA CTCTGGTACT
32761  CCAAACGCCT TCTGGCGGCA AACTTCCTCC ACACCCTGAA GGGAATGTCA GATTCTTGCT
32821  CCTGTCCCTC CGCACCCACT ATCTTCATGT TGTTGCAGAT GAAGCGCACC AAAACGTCTG
32881  ACGAGAGCTT CAACCCCGTG TACCCCTATG ACACGGAAAG CGGCCCTCCC TCCGTCCCTT
32941  TCCTCACCCC TCCCTTCGTG TCTCCCGATG GATTCCAAGA AAGCCCCCCC GGGGTCCTGT
33001  CTCTGAACCT GGCCGAGCCC CTGGTCACTT CCCACGGCAT GCTCGCCCTG AAAATGGGAA
```

Fig. 5S

SEQ ID NO:1


```
33061  GTGGCCTCTC CCTGGACGAC GCTGGCAACC TCACCTCTCA AGATATCACC ACCGCTAGCC
33121  CTCCCCTCAA AAAAACCAAG ACCAACCTCA GCCTAGAAAC CTCATCCCCC CTAACTGTAA
33181  GCACCTCAGG CGCCCTCACC GTAGCAGCCG CCGCTCCCCT GGCAGTGGCC GGCACCTCCC
33241  TCACCATGCA ATCAGAGGCC CCCCTGACAG TACAGGATGC AAAACTCACC CTGGCCACCA
33301  AAGGCCCCCT GACCGTGTCT GAAGGCAAAC TGGCCTTGCA AACATCGGCC CCGCTGACGG
33361  CCGCTGACAG CAGCACCCTC ACCGTTAGCG CCACACCACC AATTAATGTA AGCAGTGGAA
33421  GTTTAGGCTT AGACATGGAA GACCCTATGT ATACTCACGA TGGAAAACTG GGAATAAGAA
33481  TTGGGGGTCC ACTAAGAGTA GTAGACAGCT TGCACACACT CACTGTAGTT ACCGGAAATG
33541  GACTAACTGT AGATAACAAT GCCCTCCAAA CTAGAGTTAC GGGCGCCCTA GGTTATGACA
33601  CATCAGGAAA TCTACAATTG AGAGCTGCAG GAGGTATGCG AATTGATGCA AATGGCCAAC
33661  TTATCCTTAA TGTGGCATAC CCATTTGATG CTCAGAACAA TCTCAGCCTT AGACTTGGTC
33721  AGGGACCCCT GTATATAAAC ACAGACCACA ACCTGGATTT GAATTGCAAC AGAGGTCTAA
33781  CCACAACTAC CACCAACAAC ACAAAAAAAC TTGAGACTAA AATTAGCTCA GGCTTAGACT
33841  ATGACACCAA TGGTGCTGTC ATTATTAAAC TTGGCACTGG TCTAAGCTTC GACAACACAG
33901  GCGCCCTAAC TGTGGGAAAC ACTGGTGATG ATAAACTGAC TCTGTGGACG ACCCCAGACC
33961  CATCTCCAAA TTGCAGAATT CACTCAGACA AAGACTGCAA GTTTACTCTA GTCCTAACTA
34021  AGTGTGGAAG CCAAATCCTG GCCTCTGTCG CCGCCCTAGC GGTATCAGGA AATCTGGCTT
34081  CGATAACAGG CACCGTTGCC AGCGTTACCA TCTTTCTCAG ATTTGATCAG AATGGAGTGC
34141  TTATGGAAAA CTCCTCGCTA GACAGGCAGT ACTGGAACTT CAGAAATGGC AACTCAACTA
34201  ACGCTGCCCC CTACACCAAT GCAGTTGGGT TCATGCCAAA CCTCGCAGCA TACCCCAAAA
34261  CGCAAAGCCA GACTGCTAAA AACAACATTG TAAGTCAGGT TTACTTGAAT GGAGACAAAT
34321  CCAAACCCAT GACCCTTACC ATCACCCTCA ATGGAACTAA TGAATCCAGT GAAACTAGCC
34381  AGGTGAGTCA CTACTCCATG TCATTTACAT GGGCTTGGGA AAGTGGGCAA TATGCCACTG
34441  AAACCTTTGC CACCAACTCC TTCACCTTTT CTTACATTGC TGAACAATAA AAAGCATGAC
34501  ACTGATGTTC ATTTCTGATT CTTATTTTAT TATTTTCAAA CACAACAAAA TCATTCAAGT
34561  CATTCTTCCA TCTTAGCTTA ATAGACACAG TAGCTTAATA GACCCAGTAG TGCAAAGCCC
34621  CATTCTAGCT TATAGATCAG ACAGTGATAA TTAACCACCA CCACCACCAT ACCTTTTGAT
34681  TCAGGAAATC ATGATCATCA CAGGATCCTA GTCTTCAGGC CGCCCCCTCC CTCCCAAGAC
34741  ACAGAATACA CAGTCCTCTC CCCCCGACTG GCTTTAAATA ACACCATCTG GTTGGTCACA
```

Fig. 5T

SEQ ID NO:1


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34801  GACATGTTCT TAGGGGTTAT ATTCCACACG GTCTCCTGCC GCGCCAGGCG CTCGTCGGTG
34861  ATGTTGATAA ACTCTCCCGG CAGCTCGCTC AAGTTCACGT CGCTGTCCAG CGGCTGAACC
34921  TCCGGCTGAC GCGATAACTG TGCGACCGGC TGCTGGACAA ACGGAGGCCG CGCCTACAAG
34981  GGGGTAGAGT CATAATCCTC GGTCAGGATA GGGCGGTGAT GCAGCAGCAG CGAGCGAAAC
35041  ATCTGCTGCC GCCGCCGCTC CGTCCGGCAG GAAAACAACA AGCCGGTGGT CTCCTCCGCG
35101  ATAATCCGCA CCGCCCGCAG CATCAGCTTC CTCGTTCTCC GCGCGCAGCA CCTCACCCTG
35161  ATCTCGCTCA AGTCGGCGCA GTAGGTACAG CACAGCACCA CGATGTTATT CATGATCCCA
35221  CAGTGCAGGG CGCTGTATCC AAAGCTCATG CCGGGAACCA CCGCCCCCAC GTGGCCATCG
35281  TACCACAAGC GCACGTAAAT TAAGTGTCGA CCCCTCATGA ACGTGCTGGA CACAAACATT
35341  ACTTCCTTGG GCATGTTGTA ATTCACCACC TCCCGGTACC AGATAAACCT CTGGTTAAAC
35401  AGGGCACCTT CCACCACCAT CCTGAACCAA GAGGCCAGAA CCTGCCCACC GGCTATGCAC
35461  TGCAGGGAAC CCGGGTTGGA ACAATGACAA TGCAGACTCC AAGGCTCGTA ACCGTGGATC
35521  ATCCGGCTGC TGAAGGCATC GATGTTGGCA CAACACAGAC ACACGTGCAT GCACTTTCTC
35581  ATGATTAGCA GCTCTTCCCT CGTCAGGATC ATATCCCAAG GAATAACCCA TTCTTGAATC
35641  AACGTAAAAC CCACACAGCA GGGAAGGCCT CGCACATAAC TCACGTTGTG CATGGTCAGC
35701  GTGTTGCATT CTGGAAACAG CGGATGATCC TCCAGTATCG AGGCGCGGGT CTCCTTCTCA
35761  CAGGGAGGTA AAGGGTCCCT GCTGTACGGA CTGCGCCGGG ACGACCGAGA TCGTGTTGAG
35821  CGTAGTGTCA TGGAAAAGGG AACGCCGGAC GTGGTCATAC TTCTTGAAGC AGAACCAGGT
35881  TCGCGCGTGG CAGGCCTCCT TGCGTCTGCG GTCTCGCCGT CTAGCTCGCT CCGTGTGATA
35941  GTTGTAGTAC AGCCACTCCC GCAGAGCGTC GAGGCGCACC CTGGCTTCCG GATCTATGTA
36001  GACTCCGTCT TGCACCGCGG CCCTGATAAT ATCCACCACC GTAGAATAAG CAACACCCAG
36061  CCAAGCAATA CACTCGCTCT GCGAGCGGCA GACAGGAGGA GCGGGCAGAG ATGGGAGAAC
36121  CATGATAAAA AACTTTTTTT AAAGAATATT TTCCAATTCT TCGAAAGTAA GATCTATCAA
36181  GTGGCAGCGC TCCCCTCCAC TGGCGCGGTC AAACTCTACG GCCAAAGCAC AGACAACGGC
36241  ATTTCTAAGA TGTTCCTTAA TGGCGTCCAA AAGACACACC GCTCTCAAGT TGCAGTAAAC
36301  TATGAATGAA AACCCATCCG GCTGATTTTC CAATATAGAC GCGCCGGCGG CGTCCACCAA
36361  ACCCAGATAA TTTTCTTCTC TCCAGCGGTT TAGAATCTGT CTAAGCAAAT CCCTTATATC
36421  AAGTCCGGCC ATGCCAAAAA TCTGCTCAAG AGCGCCCTCC ACCTTCATGA CCAAGCAGCG
36481  CATCATGATT GCAAAAATTC AGGTTCTTCA GAGACCTGTA TAAGATTCAA AATGGGAACA
```

Fig. 5U

SEQ ID NO:1


```
36541  TTAACAAAAA TTCCTCTGTC GCGCAGATCC CTTCGCAGGG CAAGCTGAAC ATAATCAGAC
36601  AGGTCTGAAC GGACCAGTGA GGCCAAATCC CCACCAGGAA CCAGATCCAG AGACCCTATA
36661  CTGATTATGA CGCGCATACT CGGGGCTATG CTGACCAGCG TAGCGCCGAT GTAGGCGTGC
36721  TGCATGGGCG GCGAGATAAA ATGCAAAGTG CTGGTTAAAA AATCAGGCAA AGCCTCGCGC
36781  AAAAAAGCTA ACACATCATA ATCATGCTCA TGCAGGTAGT TGCAGGTAAG CTCAGGAACC
36841  AAAACGGAAT AACACACGAT TTTCCTCTCA AACATGACTT CGCGGATACT GCGTAAAACA
36901  AAAATTATAA ATAAAAAATT AATTAACTTA AACATTGGAA GCCTGTCTCA CAACAGGAAA
36961  AACCACTTTA ATCAACATAA GACGGGCCAC GGGCATGCCG GCATAGCCGT AAAAAAATTG
37021  GTCCCCGTGA TTAACAAGTA CCACAGACAG CTCCCCGGTC ATGTCGGGGG TCATCATGTG
37081  AGACTCTGTA TACACGTCTG GATTGTGAAC ATCAGACAAA CAAAGAAATC GAGCCACGTA
37141  GCCCGGAGGT ATAATCACCC GCAGGCGGAG GTACAGCAAA ACGACCCCCA TAGGAGGAAT
37201  CACAAAATTA GTAGGAGAAA AAAATACATA AACACCAGAA AAACCCTGTT GCTGAGGCAA
37261  AATAGCGCCC TCCCGATCCA AAACAACATA AAGCGCTTCC ACAGGAGCAG CCATAACAAA
37321  GACCCGAGTC TTACCAGTAA AAGAAAAAAG ATCTCTCAAC GCAGCACCAG CACCAACACT
37381  TCGCAGTGTA AAAGGCCAAG TGCCGAGAGA GTATATATAG GAATAAAAAG TGACGTAAAC
37441  GGGCAAAGTC CAAAAAACGC CCAGAAAAAC CGCACGCGAA CCTACGCCCC GAAACGAAAG
37501  CCAAAAAACA CTAGACACTC CCTTCCGGCG TCAACTTCCG CTTTCCCACG CTACGTCACT
37561  TGCCCCAGTC AAACAAACTA CATATCCCGA ACTTCCAAGT CGCCACGCCC AAAACACCGC
37621  CTACACCTCC CCGCCCGCCG GCCCGCCCCC AAACCCGCCT CCCGCCCCGC GCCCCGCCTC
37681  GCGCCGCCCA TCTCATTATC ATATTGGCTT CAATCCAAAA TAAGGTATAT TATTGATGAT
37741  G
```

Fig. 5V

SEQ ID NO:2


```
   1  CATCATCAAT AATATACCTC AAACTTTTGG TGCGCGTTAA TATGCAAATG AGCCGTTTGA
  61  ATTTGGGGAT GCGGGGCGCT GATTGGCTGC GGGAGCGGCG ACCGTTAGGG GCGGGGCGGG
 121  TGACGTTTTG ATGACGTGTT TGTGAGGCGG AGCCGGTTTG CAAGTTCTCG TGGGAAAAGT
 181  GACGTCAAAC GAGGTGTGGT TTGAACACGG AAATACTCAA TTTTCCCGCG CTCTCTGACA
 241  GGAAATGAGG TGTTTCTGGG CGGATGCAAG TGAAAACGGG CCATTTTCGC GCGAAAACTG
 301  AATGAGGAAG TGAAAATCTG AGTAATTTCG CGTTTATGGC AGGGAGGAGT ATTTGCCGAG
 361  GGCCGAGTAG ACTTTGACCG ATTACGTGGG GGTTTCGATT ACCGTATTTT TCACCTAAAT
 421  TTCCGCGTAC GGTGTCAAAG TCCGGTGTTT TTACGTAGGC GTCAGCTGAT CGCCAGGGTA
 481  TTTAAACCTG CGCTCTCTAG TCAAGAGGCC ACTCTTGAGT GCCAGCGAGT AGAGTTTTCT
 541  CCTCCGCGCC GCGAGTCAGA TCTACACTTT GAAAGATGAG GCACCTGAGA GACCTGCCCG
 601  GTAATGTTTT CCTGGCTACT GGGAACGAGA TTCTGGAACT GGTGGTGGAC GCCATGATGG
 661  GTGACGACCC TCCTGAGCCC CCTACCCCAT TTGAGGCGCC TTCGCTGTAC GATTTGTATG
 721  ATCTGGAGGT GGATGTGCCC GAGAACGACC CCAACGAGGA GGCGGTGAAT GATTTGTTTA
 781  GCGATGCCGC GCTGCTGGCC GCCGAGCAGG CTAATACGGA CTCTGGCTCA GACAGCGATT
 841  CCTCTCTCCA TACCCCGAGA CCCGGCAGAG GTGAGAAAAA GATCCCCGAG CTTAAAGGGG
 901  AAGAGCTCGA CCTGCGCTGC TATGAGGAAT GCTTGCCTCC GAGCGATGAT GAGGAGGACG
 961  AGGAGGCGAT TCGAGCTGCA GCGAGCGAGG GAGTGAAAGC TGCGGGCGAG AGCTTTAGCC
1021  TGGACTGTCC TACTCTGCCC GGACACGGCT GTAAGTCTTG TGAATTTCAT CGCATGAATA
1081  CTGGAGATAA GAATGTGATG TGTGCCCTGT GCTATATGAG AGCTTACAAC CATTGTGTTT
1141  ACAGTAAGTG TGATTAACTT TAGCTGGGAA GGCAGAGGGT GACTGGGTGC TGACTGGTTT
1201  ATTTATGTAT ATGTTTTTTA TGTGTAGGTC CCGTCTCTGA CGTAGATGAG ACCCCCACTT
1261  CAGAGTGCAT TTCATCACCC CCAGAAATTG GCGAGGAACC GCCCGAAGAT ATTATTCATA
1321  GACCAGTTGC AGTGAGAGTC ACCGGGCGGA GAGCAGCTGT GGAGAGTTTG GATGACTTGC
1381  TACAGGGTGG GGATGAACCT TTGGACTTGT GTACCCGGAA ACGCCCCAGG CACTAAGTGC
1441  CACACATGTG TGTTTACTTA AGGTGATGTC AGTATTTATA GGGTGTGGAG TGCAATAAAA
1501  TCCGTGTTGA CTTTAAGTGT GTGGTTTATG ACTCAGGGGT GGGGACTGTG GGTATATAAG
1561  CAGGTGCAGA CCTGTGTGGT CAGTTCAGAG CAGGACTCAT GGAGATCTGG ACGGTCTTGG
1621  AAGACTTTCA CCAGACTAGA CAGCTGCTAG AGAACTCATC GGAGGAAGTC TCTTACCTGT
1681  GGAGATTTTG CTTCGGTGGG GCTCTAGCTA AGCTAGTCTA TAGGGCCAAA CAGGATTATA
```

Fig. 6A

SEQ ID NO:2


```
1741  AGGATCAATT TGAGGATATT TTGAGAGAGT GTCCTAGTAT TTTTGACTCT CTCAACTTGG
1801  GCCATCAGTC TCACTTTAAC CAGAGTATTC TGAGAGCCCT TGACTTTTCT ACTCCTGGCA
1861  GAACTACCGC CGCGGTAGCC TTTTTTGCCT TTATTCTTGA CAAATGGAGT CAAGAAACCC
1921  ATTTCAGCAG GGATTACCGT CTGGACTGCT TAGCAGTAGC TTTGTGGAGA ACATGGAGGT
1981  GCCAGCGCCT GAATGCAATC TCCGGCTACT TGCCAGTACA GCCGGTAGAC ACGCTGAGGA
2041  TCCTGAGTCT CCAGTCACCC CAGGAACACC AACGCCGCCA GCAGCCGCAG CAGGAGCAGC
2101  AGCAAGAGGA GGAGGAGGAG GAGGACCGAG AAGAGAACCC GAGAGCCGGT CTGGACCCTC
2161  CGGTGGCGGA GGAGGAGGAG TAGCTGACTT GTTTCCCGAG CTGCGCCGGG TGCTGACTAG
2221  GTCTTCCAGT GGACGGGAGA GGGGGATTAA GCGGGAGAGG CATGAGGAGA CTAGTCACAG
2281  AACTGAACTG ACTGTCAGTC TGATGAGCCG CAGGCGCCCA GAATCGGTGT GGTGGCATGA
2341  GGTTCAGTCG CAGGGGATAG ATGAGGTCTC GGTAATGCAT GAGAAATATT CCCTAGAACA
2401  AGTCAAGACT TGTTGGTTGG AGCCCGAGGA TGATTGGGAG GTAGCCATCA GGAATTATGC
2461  CAAGCTGGCT CTGAGGCCAG ACAAGAAGTA CAAGATTACC AAACTGATTA ATATCAGAAA
2521  TTCCTGCTAC ATTTCGGGGA ATGGGGCCGA GGTGGAGATC AGTACCCAGG AGAGGGTGGC
2581  CTTCAGATGT TGTATGATGA ATATGTACCC GGGGGTGGTG GGCATGGAGG GAGTCACCTT
2641  TATGAACGCG AGGTTTAGGG GTGATGGGTA TAATGGGGTG GTCTTTATGG CCAACACCAA
2701  GCTGACAGTG CACGGATGCT CCTTCTTTGG CTTCAATAAC ATGTGCATCG AGGCCTGGGG
2761  CAGTGTTTCA GTGAGGGGAT GCAGCTTTTC AGCCAACTGG ATGGGGGTCG TGGGCAGAAC
2821  CAAGAGCGTG GTGTCAGTGA AGAAATGCCT GTTCGAGAGG TGCCACCTGG GGGTGATGAG
2881  CGAGGGCGAA GCCAAAGTCA AACACTGCGC CTCTACCGAG ACGGGCTGCT TTGTGATGAT
2941  CAAGGGCAAT GCCAAAGTCA AGCATAACAT GATTTGTGGG GCCTCGGATG AGCGCGGCTA
3001  CCAGATGCTG ACCTGTGCCG GTGGGAACAG CCATATGCTG GCCACCGTGC ATGTGGCCTC
3061  GCACCCCCGC AAGACATGGC CCGAGTTCGA GCACAACGTC ATGACCCGCT GCAATGTGCA
3121  CCTGGGGTCC CGCCGAGGCA TGTTCATGCC CTACCAGTGC AACATGCAAT TTGTGAAGGT
3181  GCTGCTGGAG CCCGATGCCA TGTCCAGAGT GAGCCTGGTG GGGGTGTTTG ACATGAATGT
3241  GGAGGTGTGG AAAATTCTGA GATATGATGA ATCCAAGACC AGGTGCCGGG CCTGCGAATG
3301  CGGAGGCAAG CACGCCAGGC TTCAGCCCGT GTGTGTGGAG GTGACGGAGG ACCTGCGACC
3361  CGATCATTTG GTGTTGTCCT GCAACGGGAC GGAGTTCGGC TCCAGCGGGG AAGAATCTGA
3421  CTAGAGTGAG TAGTGTTTGG GGGTGGGTGG GAGTCTGCAT GATGGGCAGA ATGACTAAAA
```

Fig. 6B

SEQ ID NO:2


```
3481  TCTGTGTTTT TCTGCGCAGC AGCATGAGCG GAAGCGCCTC CTTTGAGGGA GGGGTATTCA
3541  GCCCTTATCT GACGGGGCGT CTCCCCTCCT GGGCGGGAGT GCGTCAGAAT GTGATGGGAT
3601  CCACGGTGGA CGGCCGGCCC GTGCAGCCCG CGAACTCTTC AACCCTGACC TACGCGACCC
3661  TGAGCTCCTC GTCCGTGGAC GCAGCTGCCG CCGCAGCTGC TGCTTCCGCC GCCAGCGCCG
3721  TGCGCGGAAT GGCCTTGGGC GCCGGCTACT ACAGCTCTCT GGTGGCCAAC TCGAGTTCCA
3781  CCAATAATCC CGCCAGCCTG AACGAGGAGA AGCTGCTGCT GCTGATGGCC CAGCTCGAGG
3841  CCCTGACCCA GCGCCTGGGC GAGCTGACCC AGCAGGTGGC TCAGCTGCAG GCGGAGACGC
3901  GGGCCGCGGT TGCCACGGTG AAAACCAAAT AAAAAATGAA TCAATAAATA AACGGAGACG
3961  GTTGTTGATT TTAACACAGA GTCTTGATCT TTATTTGATT TTTCGCGCGC GGTAGGCCCT
4021  GGACCACCGG TCTCGATCAT TGAGCACCCG GTGGATTTTT TCCAGGACCC GGTAGAGGTG
4081  GGCTTGGATG TTGAGGTACA TGGGCATGAG CCCGTCCCGG GGGTGGAGGT AGCTCCATTG
4141  CAGGGCCTCG TGCTCGGGGG TGGTGTTGTA AATCACCCAG TCATAGCAGG GGCGCAGGGC
4201  GTGGTGCTGC ACGATGTCCT TGAGGAGGAG ACTGATGGCC ACGGGCAGCC CCTTGGTGTA
4261  GGTGTTGACG AACCTGTTGA GCTGGGAGGG ATGCATGCGG GGGGAGATGA GATGCATCTT
4321  GGCCTGGATC TTGAGATTGG CGATGTTCCC GCCCAGATCC CGCCGGGGGT TCATGTTGTG
4381  CAGGACCACC AGCACGGTGT ATCCGGTGCA CTTGGGGAAT TTGTCATGCA ACTTGGAAGG
4441  GAAGGCGTGA AAGAATTTGG AGACGCCCTT GTGACCGCCC AGGTTTTCCA TGCACTCATC
4501  CATGATGATG GCGATGGGCC CGTGGGCGGC GGCCTGGGCA AAGACGTTTC GGGGGTCGGA
4561  CACATCGTAG TTGTGGTCCT GGGTGAGCTC GTCATAGGCC ATTTTAATGA ATTTGGGGCG
4621  GAGAGTGCCC GACTGGGGGA CGAAGGTGCC CTCGATCCCG GGGGCGTAGT TCCCCTCGCA
4681  GATCTGCATC TCCCAGGCCT TGAGCTCGGA GGGGGGGATC ATGTCCACCT GCGGGGCGAT
4741  GAAAAAAACG GTTTCCGGGG CGGGGGAGAT GAGCTGGGCC GAAAGCAGGT TCCGGAGCAG
4801  CTGGGACTTG CCGCAGCCGG TGGGACCGTA GATGACCCCG ATGACCGGCT GCAGGTGGTA
4861  GTTGAGGGAG AGACAGCTGC CATCCTCGCG GAGGAGGGGG GCCACCTCGT TCATCATCTC
4921  GCGCACATGC ATGTTCTCGC GCACGAGTTC CGCCAGGAGG CGCTCGCCCC CCAGCGAGAG
4981  GAGCTCTTGC AGCGAGGCGA AGTTTTTCAG CGGCTTGAGC CCGTCGGCCA TGGGCATTTT
5041  GGAGAGGGTC TGTTGCAAGA GTTCCAGACG GTCCCAGAGC TCGGTGATGT GCTCTAGGGC
5101  ATCTCGATCC AGCAGACCTC CTCGTTTCGC GGGTTGGGGC GACTGCGGGA GTAGGGCACC
5161  AGGCGATGGG CGTCCAGCGA GGCCAGGGTC CGGTCCTTCC AGGGTCGCAG GGTCCGCGTC
```

Fig. 6C

```
5221  AGCGTGGTCT CCGTCACGGT GAAGGGGTGC GCGCCGGGCT GGGCGCTTGC GAGGGTGCGC
5281  TTCAGGCTCA TCCGGCTGGT CGAGAACCGC TCCCGGTCGG CGCCCTGCGC GTCGGCCAGG
5341  TAGCAATTGA GCATGAGTTC GTAGTTGAGC GCCTCGGCCG CGTGGCCCTT GGCGCGGAGC
5401  TTACCTTTGG AAGTGTGTCC GCAGACGGGA CAGAGGAGGG ACTTGAGGGC GTAGAGCTTG
5461  GGGGCGAGGA AGACGGACTC GGGGGCGTAG GCGTCCGCGC CGCAGCTGGC GCAGACGGTC
5521  TCGCACTCCA CGAGCCAGGT GAGGTCGGGG CGGTCGGGGT CAAAAACGAG GTTTCCTCCG
5581  TGCTTTTTGA TGCGTTTCTT ACCTCTGGTC TCCATGAGCT CGTGTCCCCG CTGGGTGACA
5641  AAGAGGCTGT CCGTGTCCCC GTAGACCGAC TTTATGGGCC GGTCCTCGAG CGGGGTGCCG
5701  CGGTCCTCGT CGTAGAGGAA CCCCGCCCAC TCCGAGACGA AGGCCCGGGT CCAGGCCAGC
5761  ACGAAGGAGG CCACGTGGGA GGGGTAGCGG TCGTTGTCCA CCAGCGGGTC CACCTTCTCC
5821  AGGGTATGCA AGCACATGTC CCCCTCGTCC ACATCCAGGA AGGTGATTGG CTTGTAAGTG
5881  TAGGCCACGT GACCGGGGGT CCCGGCCGGG GGGGTATAAA AGGGGGCGGG CCCCTGCTCG
5941  TCCTCACTGT CTTCCGGATC GCTGTCCAGG AGCGCCAGCT GTTGGGGTAG GTATTCCCTC
6001  TCGAAGGCGG GCATGACCTC GGCACTCAGG TTGTCAGTTT CTAGAAACGA GGAGGATTTG
6061  ATATTGACGG TGCCGTTGGA GACGCCTTTC ATGAGCCCCT CGTCCATCTG GTCAGAAAAG
6121  ACGATCTTTT TGTTGTCGAG CTTGGTGGCG AAGGAGCCGT AGAGGGCGTT GGAGAGGAGC
6181  TTGGCGATGG AGCGCATGGT CTGGTTCTTT TCCTTGTCGG CGCGCTCCTT GGCGGCGATG
6241  TTGAGCTGCA CGTACTCGCG CGCCACGCAC TTCCATTCGG GGAAGACGGT GGTGAGCTCG
6301  TCGGGCACGA TTCTGACCCG CCAGCCGCGG TTGTGCAGGG TGATGAGGTC CACGCTGGTG
6361  GCCACCTCGC CGCGCAGGGG CTCGTTGGTC CAGCAGAGGC GCCCGCCCTT GCGCGAGCAG
6421  AAGGGGGGCA GCGGGTCCAG CATGAGCTCG TCTGGGGGGT CGGCGTCCAC GGTGAAGATG
6481  CCGGGCAGGA GCTCGGGGTC GAAGTAGCTG ATGGAAGTGG CCAGATCGTC CAGGGAAGCT
6541  TGCCAGTCGC GCACGGCCAG CGCGCGCTCG TAGGGGCTGA GGGGCGTGCC CCAGGGCATG
6601  GGGTGCGTGA GCGCGGAGGC GTACATGCCG CAGATGTCGT AGACGTAGAG GGGCTCCTCG
6661  AGGATGCCGA TGTAGGTGGG GTAGCAGCGC CCCCCGCGGA TGCTGGCGCG CACGTAGTCG
6721  TACAGCTCGT GCGAGGGCGC GAGGAGCCCC GTGCCGAGAT TGGAGCGCTG CGGCTTTTCG
6781  GCGCGGTAGA CGATCTGGCG GAAGATGGCG TGGGAGTTGG AGGAGATGGT GGGCCTCTGG
6841  AAGATGTTGA AGTGGGCGTG GGGCAGGCCG ACCGAGTCCC TGATGAAGTG GGCGTAGGAG
6901  TCCTGCAGCT TGGCGACGAG CTCGGCGGTG ACGAGGACGT CCAGGGCGCA GTAGTCGAGG
```

Fig. 6D

SEQ ID NO:2


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6961  GTCTCTTGGA TGATGTCATA CTTGAGCTGG CCCTTCTGCT TCCACAGCTC GCGGTTGAGA
7021  AGGAACTCTT CGCGGTCCTT CCAGTACTCT TCGAGGGGGA ACCCGTCCTG ATCGGCACGG
7081  TAAGAGCCCA CCATGTAGAA CTGGTTGACG GCCTTGTAGG CGCAGCAGCC CTTCTCCACG
7141  GGGAGGGCGT AAGCTTGCGC GGCCTTGCGC AGGGAGGTGT GGGTGAGGGC GAAGGTGTCG
7201  CGCACCATGA CCTTGAGGAA CTGGTGCTTG AAGTCGAGGT CGTCGCAGCC GCCCTGCTCC
7261  CAGAGTTGGA AGTCCGTGCG CTTCTTGTAG GCGGGGTTGG GCAAAGCGAA AGTAACATCG
7321  TTGAAGAGGA TCTTGCCCGC GCGGGGCATG AAGTTGCGAG TGATGCGGAA AGGCTGGGGC
7381  ACCTCGGCCC GGTTGTTGAT GACCTGGGCG GCGAGGACGA TCTCGTCGAA GCCGTTGATG
7441  TTGTGCCCGA CGATGTAGAG TTCCACGAAT CGCGGGCGGC CCTTGACGTG GGGCAGCTTC
7501  TTGAGCTCGT CGTAGGTGAG CTCGGCGGGG TCGCTGAGCC CGTGCTGTTC GAGGGCCCAG
7561  TCGGCGACGT GGGGGTTGGC GCTGAGGAAG GAAGTCCAGA GATCCACGGC CAGGGCGGTC
7621  TGCAAGCGGT CCCGGTACTG ACGGAACTGC TGGCCCACGG CCATTTTTTC GGGGGTGACG
7681  CAGTAGAAGG TGCGGGGGTC GCCGTGCCAG CGGTCCCACT TGAGCTGGAG GGCGAGGTCG
7741  TGGGCGAGCT CGACGAGCGG TGGGTCCCCG GAGAGTTTCA TGACCAGCAT GAAGGGGACG
7801  AGCTGCTTGC CGAAGGACCC CATCCAGGTG TAGGTTTCCA CATCGTAGGT GAGGAAGAGC
7861  CTTTCGGTGC GAGGATGCGA GCCGATGGGG AAGAACTGGA TCTCCTGCCA CCAGTTGGAG
7921  GAATGGCTGT TGATGTGATG GAAGTAGAAA TGCCGACGGC GCGCCGAGCA CTCGTGCTTG
7981  TGTTTATACA AGCGTCCGCA GTGCTCGCAA CGCTGCACGG GATGCACGTG CTGCACGAGC
8041  TGTACCTGAG TTCCTTTGAC GAGGAATTTC AGTGGGCAGT GGAGCGCTGG CGGCTGCATC
8101  TGGTGCTGTA CTACGTCCTG GCCATCGGCG TGGCCATCGT CTGCCTCGAT GGTGGTCATG
8161  CTGACGAGGC CGCGCGGGAG GCAGGTCCAG ACCTCGGCTC GGACGGGTCG GAGAGCGAGG
8221  ACGAGGGCGC GCAGGCCGGA GCTGTCCAGG GTCCTGAGAC GCTGCGGAGT CAGGTCAGTG
8281  GGCAGCGGCG GCGCGCGGTT GACTTGCAGG AGCTTTTCCA GGGCGCGCGG GAGGTCCAGA
8341  TGGTACTTGA TCTCCACGGC GCCGTTGGTG GCGACGTCCA CGGCTTGCAG GGTCCCGTGC
8401  CCCTGGGGCG CCACCACCGT GCCCCGTTTC TTCTTGGGCG CTGGTTCCAT GCCGGTCAGA
8461  AGCGGCGGCG AGGACGCGCG CCGGGCGGCA GGGGCGGCTC GGGGCCCGGA GGCAGGGGCG
8521  GCAGGGGCAC GTCGGCGCCG CGCGCGGGCA GGTTCTGGTA CTGCGCCCGG AGAAGACTGG
8581  CGTGAGCGAC GACGCGACGG TTGACGTCCT GGATCTGACG CCTCTGGGTG AAGGCCACGG
8641  GACCCGTGAG TTTGAACCTG AAAGAGAGTT CGACAGAATC AATCTCGGTA TCGTTGACGG
```

Fig. 6E

SEQ ID NO:2


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 8701  CGGCCTGCCG CAGGATCTCT TGCACGTCGC CCGAGTTGTC CTGGTAGGCG ATCTCGGTCA
 8761  TGAACTGCTC GATCTCCTCC TCCTGAAGGT CTCCGCGGCC GGCGCGCTCG ACGGTGGCCG
 8821  CGAGGTCGTT GGAGATGCGG CCCATGAGCT GCGAGAAGGC GTTCATGCCG GCCTCGTTCC
 8881  AGACGCGGCT GTAGACCACG GCTCCGTCGG GGTCGCGCGC GCGCATGACC ACCTGGGCGA
 8941  GGTTGAGCTC GACGTGGCGC GTGAAGACCG CGTAGTTGCA GAGGCGCTGG TAGAGGTAGT
 9001  TGAGCGTGGT GGCGATGTGC TCGGTGACGA AGAAGTACAT GATCCAGCGG CGGAGCGGCA
 9061  TCTCGCTGAC GTCGCCCAGG GCTTCCAAGC GCTCCATGGC CTCGTAGAAG TCCACGGCGA
 9121  AGTTGAAAAA CTGGGAGTTG CGCGCCGAGA CGGTCAACTC CTCCTCCAGA AGACGGATGA
 9181  GCTCGGCGAT GGTGGCGCGC ACCTCGCGCT CGAAGGCCCC GGGGGGCTCC TCTTCTTCCA
 9241  TCTCCTCCTC CTCTTCCTCC TCCACTAACA TCTCTTCTAC TTCCTCCTCA GGAGGCGGTG
 9301  GCGGGGGAGG GGCCCTGCGT CGCCGGCGGC GCACGGGCAG ACGGTCGATG AAGCGCTCGA
 9361  TGGTCTCCCC GCGCCGGCGA CGCATGGTCT CGGTGACGGC GCGCCCGTCC TCGCGGGGCC
 9421  GCAGCGTGAA GACGCCGCCG CGCATCTCCA GGTGGCCGCC GGGGGGGTCT CCGTTGGGCA
 9481  GGGAGAGGGC GCTGACGATG CATCTTATCA ATTGGCCCGT AGGGACTCCG CGCAAGGACC
 9541  TGAGCGTCTC GAGATCCACG GGATCCGAAA ACCGCTGAAC GAAGGCTTCG AGCCAGTCGC
 9601  AGTCGCAAGG TAGGCTGAGC CCGGTTTCTT CGGGTATTTG GTCGGGAGGC GGGCGGGCGA
 9661  TGCTGCTGGT GATGAAGTTG AAGTAGGCGG TCCTGAGACG GCGGATGGTG GCGAGGAGCA
 9721  CCAGGTCCTT GGGCCCGGCT TGCTGGATGC GCAGACGGTC GGCCATGCCC CAGGCGTGGT
 9781  CCTGACACCT GGCGAGGTCC TTGTAGTAGT CCTGCATGAG CCGCTCCACG GGCACCTCCT
 9841  CCTCGCCCGC GCGGCCGTGC ATGCGCGTGA GCCCGAACCC GCGCTGCGGC TGGACGAGCG
 9901  CCAGGTCGGC GACGACGCGC TCGGCGAGGA TGGCCTGCTG GATCTGGGTG AGGGTGGTCT
 9961  GGAAGTCGTC GAAGTCGACG AAGCGGTGGT AGGCTCCGGT GTTGATGGTG TATGAGCAGT
10021  TGGCCATGAC GGACCAGTTG ACGGTCTGGT GGCCGGGGCG CACGAGCTCG TGGTACTTGA
10081  GGCGCGAGTA GGCGCGCGTG TCGAAGATGT AGTCGTTGCA GGTGCGCACG AGGTACTGGT
10141  ATCCGACGAG GAAGTGCGGC GGCGGCTGGC GGTAGAGCGG CCATCGCTCG GTGGCGGGGG
10201  CGCCGGGCGC GAGGTCCTCG AGCATGAGGC GGTGGTAGCC GTAGATGTAC CTGGACATCC
10261  AGGTGATGCC GGCGGCGGTG GTGGAGGCGC GCGGGAACTC GCGGACGCGG TTCCAGATGT
10321  TGCGCAGCGG CAGGAAGTAG TTCATGGTGG CCGCGGTCTG GCCCGTGAGG CGCGCGCAGT
10381  CGTGGATGCT CTATACGGGC AAAAACGAAA GCGGTCAGCG GCTCGACTCC GTGGCCTGGA
```

Fig. 6F

SEQ ID NO:2


```
10441  GGCTAAGCGA ACGGGTTGGG CTGCGCGTGT ACCCCGGTTC GAATCTCGAA TCAGGCTGGA
10501  GCCGCAGCTA ACGTGGTACT GGCACTCCCG TCTCGACCCA AGCCTGCACA AAACCTCCAG
10561  GATACGGAGG CGGGTCGTTT TGCAACTTTT TGAGGCCGGA AATGAAACTA GTAAGCGCGA
10621  AAAGCGGCCG ACCGCGATGG CTCGCTGCCG TAGTCTGGAG AAGAATCGCC AGGGTTGCGT
10681  TGCGGTGTGC CCCGGTTCGA GGCCGGCCGG ATTCCGCGGC TAACGAGGGC GTGGCTGCCC
10741  CGTCGTTTCC AAGACCCCTA GCCAGCCGAC TTCTCCAGTT ACGGAGCGAG CCCCTCTTTT
10801  GTTTTGTTTG TTTTTGCCAG ATGCATCCCG TACTGCGGCA GATGCGCCCC CACCACCCTC
10861  CACCGCAACA ACAGCCCACT CCACAGCCGG CGCTTCTGCC CCCGCCCCAG CAGCAGCAAC
10921  TTCCAGCCAC GACCGCCGCG GCCGCCGTGA GCGGGGCTGG ACAGACTTCT CAGTATGACC
10981  ACCTGGCCTT GGAAGAGGGC GAGGGGCTGG CGCGCCTGGG GGCGTCGTCG CCGGAGCGGC
11041  ACCCGCGCGT GCAGATGAAA CGGGACGCTC GCGAGGCCTA CGTGCCCAAG CAGAACCTGT
11101  TCAGAGACAG GAGCGGCGAG GAGCCCGAGG AGATGCGCGC GGCCCGGTTC CACGCGGGGC
11161  GGGAGCTGCG GCGCGGCCTG GACCGAAAGA GGGTGCTGAG GGACGAGGAT TTCGAGGCGG
11221  ACGAGCTGAC GGGGATCAGC CCCGCGCGCG CGCACGTGGC CGCGGCCAAC CTGGTCACGG
11281  CGTACGAGCA GACCGTGAAG GAGGAGAGCA ACTTCCAAAA ATCCTTCAAC AACCACGTGC
11341  GCACCCTGAT CGCGCGCGAG GAGGTGACCC TGGGCCTGAT GCACCTGTGG GACCTGCTGG
11401  AGGCCATCGT GCAGAACCCC ACCAGCAAGC CGCTGACGGC GCAGCTGTTC CTGGTGGTGC
11461  AGCACAGTCG GGACAACGAG GCGTTCAGGG AGGCGCTGCT GAATATCACC GAGCCCGAGG
11521  GCCGCTGGCT CCTGGACCTG GTGAACATTC TGCAGAGCAT CGTGGTGCAG GAGCGCGGGC
11581  TGCCGCTGTC CGAGAAGCTG GCGGCCATCA ACTTCTCGGT GCTGAGTCTG GGCAAGTACT
11641  ACGCTAGGAA GATCTACAAG ACCCCGTACG TGCCCATAGA CAAGGAGGTG AAGATCGACG
11701  GGTTTTACAT GCGCATGACC CTGAAAGTGC TGACCCTGAG CGACGATCTG GGGGTGTACC
11761  GCAACGACAG GATGCACCGC GCGGTGAGCG CCAGCCGCCG GCGCGAGCTG AGCGACCAGG
11821  AGCTGATGCA CAGCCTGCAG CGGGCCCTGA CCGGGGCCGG GACCGAGGGG GAGAGCTACT
11881  TTGACATGGG CGCGGACCTG CGCTGGCAGC CCAGCCGCCG GGCCTTGGAA GCTGCCGGCG
11941  GTTCCCCCTA CGTGGAGGAG GTGGACGATG AGGAGGAGGA GGGCGAGTAC CTGGAAGACT
12001  GATGGCGCGA CCGTATTTTT GCTAGATGCA GCAACAGCCA CCGCCGCCTC CTGATCCCGC
12061  GATGCGGGCG GCGCTGCAGA GCCAGCCGTC CGGCATTAAC TCCTCGGACG ATTGGACCCA
12121  GGCCATGCAA CGCATCATGG CGCTGACGAC CCGCAATCCC GAAGCCTTTA GACAGCAGCC
```

Fig. 6G

SEQ ID NO:2


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12181  TCAGGCCAAC CGGCTCTCGG CCATCCTGGA GGCCGTGGTG CCCTCGCGCT CGAACCCCAC
12241  GCACGAGAAG GTGCTGGCCA TCGTGAACGC GCTGGTGGAG AACAAGGCCA TCCGCGGCGA
12301  CGAGGCCGGG CTGGTGTACA ACGCGCTGCT GGAGCGCGTG GCCCGCTACA ACAGCACCAA
12361  CGTGCAGACG AACCTGGACC GCATGGTGAC CGACGTGCGC GAGGCGGTGT CGCAGCGCGA
12421  GCGGTTCCAC CGCGAGTCGA ACCTGGGCTC CATGGTGGCG CTGAACGCCT TCCTGAGCAC
12481  GCAGCCCGCC AACGTGCCCC GGGGCCAGGA GGACTACACC AACTTCATCA GCGCGCTGCG
12541  GCTGATGGTG GCCGAGGTGC CCCAGAGCGA GGTGTACCAG TCGGGGCCGG ACTACTTCTT
12601  CCAGACCAGT CGCCAGGGCT TGCAGACCGT GAACCTGAGC CAGGCTTTCA AGAACTTGCA
12661  GGGACTGTGG GGCGTGCAGG CCCCGGTCGG GGACCGCGCG ACGGTGTCGA GCCTGCTGAC
12721  GCCGAACTCG CGCCTGCTGC TGCTGCTGGT GGCGCCCTTC ACGGACAGCG GCAGCGTGAG
12781  CCGCGACTCG TACCTGGGCT ACCTGCTTAA CCTGTACCGC GAGGCCATCG GGCAGGCGCA
12841  CGTGGACGAG CAGACCTACC AGGAGATCAC CCACGTGAGC CGCGCGCTGG GCCAGGAGGA
12901  CCCGGGCAAC CTGGAGGCCA CCCTGAACTT CCTGCTGACC AACCGGTCGC AGAAGATCCC
12961  GCCCCAGTAC GCGCTGAGCA CCGAGGAGGA GCGCATCCTG CGCTACGTGC AGCAGAGCGT
13021  GGGGCTGTTC CTGATGCAGG AGGGGGCCAC GCCCAGCGCC GCGCTCGACA TGACCGCGCG
13081  CAACATGGAG CCCAGCATGT ACGCCCGCAA CCGCCCGTTC ATCAATAAGC TGATGGACTA
13141  CTTGCATCGG GCGGCCGCCA TGAACTCGGA CTACTTTACC AACGCCATCT TGAACCCGCA
13201  CTGGCTCCCG CCGCCCGGGT TCTACACGGG CGAGTATGAC ATGCCCGACC CCAACGACGG
13261  GTTCCTGTGG GATGACGTGG ACAGCAGCGT GTTCTCGCCG CGCCCCGCCA CCACCGTGTG
13321  GAAGAAAGAG GGCGGGGACC GGCGGCCGTC CTCGGCGCTG TCCGGTCGCG CGGGTGCTGC
13381  CGCGGCGGTG CCCGAGGCCG CCAGCCCCTT CCCGAGCCTG CCCTTTTCGC TGAACAGCGT
13441  GCGCAGCAGC GAGCTGGGAC GGCTGACGCG GCCGCGCCTG CTGGGCGAGG AGGAGTACCT
13501  GAACGACTCC TTGTTGAGGC CCGAGCGCGA GAAGAACTTC CCCAATAACG GGATAGAGAG
13561  CCTGGTGGAC AAGATGAGCC GCTGGAAGAC GTACGCGCAC GAGCACAGGG ACGAGCCGCG
13621  AGCTAGCAGC AGCACCGGCG CCCGTAGACG CCAGCGGCAC GACAGGCAGC GGGGACTGGT
13681  GTGGGACGAT GAGGATTCCG CCGACGACAG CAGCGTGTTG GACTTGGGTG GGAGTGGTGG
13741  TGGTAACCCG TTCGCTCACC TGCGCCCCCG TATCGGGCGC CTGATGTAAG AATCTGAAAA
13801  AATAAAAAAC GGTACTCACC AAGGCCATGG CGACCAGCGT GCGTTCTTCT CTGTTGTTTG
13861  TAGTAGTATG ATGAGGCGCG TGTACCCGGA GGGTCCTCCT CCCTCGTACG AGAGCGTGAT
```

Fig. 6H

SEQ ID NO:2


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13921  GCAGCAGGCG GTGGCGGCGG CGATGCAGCC CCCGCTGGAG GCGCCTTACG TGCCCCCGCG
13981  GTACCTGGCG CCTACGGAGG GGCGGAACAG CATTCGTTAC TCGGAGCTGG CACCCTTGTA
14041  CGATACCACC CGGTTGTACC TGGTGGACAA CAAGTCGGCG GACATCGCCT CGCTGAACTA
14101  CCAGAACGAC CACAGCAACT TCCTGACCAC CGTGGTGCAG AACAACGATT TCACCCCCAC
14161  GGAGGCCAGC ACCCAGACCA TCAACTTTGA CGAGCGCTCG CGGTGGGGCG GCCAGCTGAA
14221  AACCATCATG CACACCAACA TGCCCAACGT GAACGAGTTC ATGTACAGCA ACAAGTTCAA
14281  GGCGCGGGTC ATGGTCTCGC GCAAGACCCC CAACGGGGTC GCGGTAGGGG ATGATTATGA
14341  TGGTAGTCAG GACGAGCTGA CCTACGAGTG GGTGGAGTTT GAGCTGCCCG AGGGCAACTT
14401  CTCGGTGACC ATGACCATCG ATCTGATGAA CAACGCCATC ATCGACAATT ACTTGGCGGT
14461  GGGACGGCAG AACGGGGTGC TGGAGAGCGA CATCGGCGTG AAGTTCGACA CGCGCAACTT
14521  CCGGCTGGGC TGGGACCCCG TGACCGAGCT GGTGATGCCG GGCGTGTACA CCAACGAGGC
14581  CTTCCACCCC GACATCGTCC TGCTGCCCGG CTGCGGCGTG GACTTCACCG AGAGCCGCCT
14641  CAGCAACCTG CTGGGCATCC GCAAGCGGCA GCCCTTCCAG GAGGGCTTCC AGATCCTGTA
14701  CGAGGACCTG GAGGGGGGCA ACATCCCCGC GCTCTTGGAT GTCGAAGCCT ATGAAGAAAG
14761  TAAGGAAAAA GCAGAGGCTG AGGCAACTGC AGCCGTGGCT ACTGCCGCTG TCACCGATGC
14821  AGATGCAGCT ACTACCAGGG GCGATACATT CGCCACTGTG GCTGAAGAAG CAGCCGCCGT
14881  AGCGGCGACC GATGATAGTG AAAGTAAGAT AGTCATCAAG CCGGTGGAGA AGGACAGCAA
14941  GAACAGGAGC TACAACGTTC TATCGGATGG AAAGAACACC GCCTACCGCA GCTGGTACCT
15001  GGCCTACAAC TACGGCGACC CCGAGAAGGG CGTGCGCTCC TGGACGCTGC TCACCACCTC
15061  GGACGTCACC TGCGGCGTGG AGCAAGTCTA CTGGTCGCTG CCCGACATGA TGCAAGACCC
15121  GGTCACCTTC CGCTCCACGC GTCAAGTTAG CAACTACCCG GTGGTGGGCG CCGAGCTCCT
15181  GCCCGTCTAC TCCAAGAGCT TCTTCAACGA GCAGGCCGTC TACTCGCAGC AGCTGCGCGC
15241  CTTCACCTCG CTCACGCACG TCTTCAACCG CTTCCCCGAG AACCAGATCC TCGTCCGCCC
15301  GCCCGCGCCC ACCATTACCA CCGTCAGTGA AAACGTTCCT GCTCTCACAG ATCACGGGAC
15361  CCTGCCGCTG CGCAGCAGTA TCCGGGGAGT CCAGCGCGTG ACCGTCACTG ACGCCAGACG
15421  CCGCACCTGC CCCTACGTCT ACAAGGCCCT GGGCGTAGTC GCGCCGCGCG TCCTCTCGAG
15481  CCGCACCTTC TAAAAAATGT CCATTCTCAT CTCGCCCAGT AATAACACCG GTTGGGGCCT
15541  GCGCGCGCCC AGCAAGATGT ACGGAGGCGC TCGCCAACGC TCCACGCAAC ACCCCGTGCG
15601  CGTGCGCGGG CACTTCCGCG CTCCCTGGGG CGCCCTCAAG GGCCGCGTGC GCTCGCGCAC
```

Fig. 6I

SEQ ID NO:2


```
15661  CACCGTCGAC GACGTGATCG ACCAGGTGGT GGCCGACGCG CGCAACTACA CGCCCGCCGC
15721  CGCGCCCGTC TCCACCGTGG ACGCCGTCAT CGACAGCGTG GTGGCCGACG CGCGCCGGTA
15781  CGCCCGCGCC AAGAGCCGGC GGCGGCGCAT CGCCCGGCGG CACCGGAGCA CCCCCGCCAT
15841  GCGCGCGGCG CGAGCCTTGC TGCGCAGGGC CAGGCGCACG GGACGCAGGG CCATGCTCAG
15901  GGCGGCCAGA CGCGCGGCCT CTGGCAGCAG CAGCGCCGGC AGGACCCGCA GACGCGCGGC
15961  CACGGCGGCG GCGGCGGCCA TCGCCAGCAT GTCCCGCCCG CGGCGCGGCA ACGTGTACTG
16021  GGTGCGCGAC GCCGCCACCG GTGTGCGCGT GCCCGTGCGC ACCCGCCCCC CTCGCACTTG
16081  AAGATGCTGA CTTCGCGATG TTGATGTGTC CCAGCGGCGA GGAGGATGTC CAAGCGCAAA
16141  TTCAAGGAAG AGATGCTCCA GGTCATCGCG CCTGAGATCT ACGGCCCCGC GGCGGCGGTG
16201  AAGGAGGAAA GAAAGCCCCG CAAACTGAAG CGGGTCAAAA AGGACAAAAA GGAGGAGGAA
16261  GATGTGGACG GACTGGTGGA GTTTGTGCGC GAGTTCGCCC CCCGGCGGCG CGTGCAGTGG
16321  CGCGGGCGGA AAGTGAAACC GGTGCTGCGA CCCGGCACCA CCGTGGTCTT CACGCCCGGC
16381  GAGCGTTCCG GCTCCGCCTC CAAGCGCTCC TACGACGAGG TGTACGGGGA CGAGGACATC
16441  CTCGAGCAGG CGGCCGAGCG TCTGGGCGAG TTTGCTTACG GCAAGCGCAG CCGCCCCGCG
16501  CCCTTGAAAG AGGAGGCGGT GTCCATCCCG CTGGACCACG GCAACCCCAC GCCGAGTCTG
16561  AAGCCGGTGA CCCTGCAGCA GGTGCTGCCG AGCGCGGCGC CGCGCCGGGG CTTCAAGCGC
16621  GAGGGCGGCG AGGATCTGTA CCCGACCATG CAGCTGATGG TGCCCAAGCG CCAGAAGCTG
16681  GAGGACGTGC TGGAGCACAT GAAGGTGGAC CCCGAGGTGC AGCCCGAGGT CAAGGTGCGG
16741  CCCATCAAGC AGGTGGCCCC GGGCCTGGGC GTGCAGACCG TGGACATCAA GATCCCCACG
16801  GAGCCCATGG AAACGCAGAC CGAGCCCGTG AAGCCCAGCA CCAGCACCAT GGAGGTGCAG
16861  ACGGATCCCT GGATGCCGGC GCCGGCTTCC ACCACCACCA CTCGCCGAAG ACGCAAGTAC
16921  GGCGCGGCCA GCCTGCTGAT GCCCAACTAC GCGCTGCATC CTTCCATCAT CCCCACGCCG
16981  GGCTACCGCG GCACGCGCTT CTACCGCGGC TACAGCAGCC GCCGCAAGAC CACCACCCGC
17041  CGCCGCCGTC GTCGCACCCG CCGCAGCAGC ACCGCGACTT CCGCCGCCTT GGTGCGGAGA
17101  GTGTACCGCA GCGGGCGCGA GCCTCTGACC CTGCCGCGCG CGCGCTACCA CCCGAGCATC
17161  GCCATTTAAC TCTGCCGTCG CCTCCTACTT GCAGATATGG CCCTCACATG CCGCCTCCGC
17221  GTCCCCATTA CGGGCTACCG AGGAAGAAAG CCGCGCCGTA GAAGGCTGAC GGGGAACGGG
17281  CTGCGTCGCC ATCACCACCG GCGGCGGCGC GCCATCAGCA AGCGGTTGGG GGGAGGCTTC
17341  CTGCCCGCGC TGATCCCCAT CATCGCCGCG GCGATCGGGG CGATCCCCGG CATAGCTTCC
```

Fig. 6J

SEQ ID NO:2


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17401  GTGGCGGTGC AGGCCTCTCA GCGCCACTGA GACACAGCTT GGAAAATTTG TAATAAAAAA
17461  TGGACTGACG CTCCTGGTCC TGTGATGTGT GTTTTTAGAT GGAAGACATC AATTTTTCGT
17521  CCCTGGCACC GCGACACGGC ACGCGGCCGT TTATGGGCAC CTGGAGCGAC ATCGGCAACA
17581  GCCAACTGAA CGGGGGCGCC TTCAATTGGA GCAGTCTCTG GAGCGGGCTT AAGAATTTCG
17641  GGTCCACGCT CAAAACCTAT GGCAACAAGG CGTGGAACAG CAGCACAGGG CAGGCGCTGA
17701  GGGAAAAGCT GAAAGAGCAG AACTTCCAGC AGAAGGTGGT CGATGGCCTG GCCTCGGGCA
17761  TCAACGGGGT GGTGGACCTG GCCAACCAGG CCGTGCAGAA ACAGATCAAC AGCCGCCTGG
17821  ACGCGGTCCC GCCCGCGGGG TCCGTGGAGA TGCCCCAGGT GGAGGAGGAG CTGCCTCCCC
17881  TGGACAAGCG CGGCGACAAG CGACCGCGTC CCGATGCAGA GGAGACGCTG CTGACGCACA
17941  CGGACGAGCC GCCCCCGTAC GAGGAGGCGG TGAAACTGGG TCTGCCCACC ACGCGGCCCG
18001  TGGCGCCTCT GGCCACCGGG GTGCTGAAAC CCAGCAGCAG CAGCCAGCCC GCGACCCTGG
18061  ACTTGCCTCC GCCTGCTTCC CGCCCCTCCA CAGTGGCTAA GCCCCTGCCG CCGGTGGCCG
18121  TCGCGTCGCG CGCCCCCCGA GGCCGCCCCC AGGCGAACTG GCAGAGCACT CTGAACAGCA
18181  TCGTGGGTCT GGGAGTGCAG AGTGTGAAGC GCCGCCGCTG CTATTAAAAG ACACTGTAGC
18241  GCTTAACTTG CTTGTCTGTG TGTATATGTA TGTCCGCCGA CCAGAAGGAA GAGGCGCGTC
18301  GCCGAGTTGC AAGATGGCCA CCCCATCGAT GCTGCCCCAG TGGGCGTACA TGCACATCGC
18361  CGGACAGGAC GCTTCGGAGT ACCTGAGTCC GGGTCTGGTG CAGTTCGCCC GCGCCACAGA
18421  CACCTACTTC AGTCTGGGGA ACAAGTTTAG GAACCCCACG GTGGCGCCCA CGCACGATGT
18481  GACCACCGAC CGCAGCCAGC GGCTGACGCT GCGCTTCGTG CCCGTGGACC GCGAGGACAA
18541  CACCTACTCG TACAAAGTGC GCTACACGCT GGCCGTGGGC GACAACCGCG TGCTGGACAT
18601  GGCCAGCACC TACTTTGACA TCCGCGGCGT GCTGGATCGG GGCCCCAGCT TCAAACCCTA
18661  CTCCGGCACC GCCTACAACA GCCTGGCTCC CAAGGGAGCG CCCAACACCT CACAGTGGAT
18721  AACCAAAGAC AATGGAACTG ATAAGACATA CAGTTTTGGA AATGCTCCAG TCAGAGGATT
18781  GGACATTACA GAAGAGGGTC TCCAAATAGG ACCCGATGAG TCAGGGGGTG AAAGCAAGAA
18841  AATTTTTGCA GACAAAACCT ATCAGCCTGA ACCTCAGCTT GGAGATGAGG AATGGCATGA
18901  TACTATTGGA GCTGAAGACA AGTATGGAGG CAGAGCGCTT AAACCTGCCA CCAACATGAA
18961  ACCCTGCTAT GGGTCTTTCG CCAAGCCAAC TAATGCTAAG GGAGGTCAGG CTAAAAGCAG
19021  AACCAAGGAC GATGGCACTA CTGAGCCTGA TATTGACATG GCCTTCTTTG ACGATCGCAG
19081  TCAGCAAGCT AGTTTCAGTC CAGAACTTGT TTTGTATACT GAGAATGTCG ATCTGGACAC
```

Fig. 6K

SEQ ID NO:2

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19141  CCCGGATACC CACATTATTT ACAAACCTGG CACTGATGAA ACAAGTTCTT CTTTCAACTT
19201  GGGTCAGCAG TCCATGCCCA ACAGACCCAA CTACATCGGC TTCAGAGACA ACTTTATCGG
19261  TCTCATGTAC TACAACAGTA CTGGCAATAT GGGTGTACTA GCTGGACAGG CCTCCCAGCT
19321  GAATGCTGTG GTGGACTTGC AGGACAGAAA CACTGAACTG TCCTACCAGC TCTTGCTTGA
19381  CTCTCTGGGT GACAGAACCA GGTATTTCAG TATGTGGAAC CAGGCGGTGG ACAGCTACGA
19441  CCCCGATGTG CGCATTATTG AAAATCACGG TGTGGAGGAT GAACTACCCA ACTATTGCTT
19501  CCCTTTGAAT GGTGTGGGCT TTACAGATAC ATTCCAGGGA ATTAAGGTTA AAACTACCAA
19561  TAACGGAACA GCAAATGCTA CAGAGTGGGA ATCTGATACC TCTGTCAATA ATGCTAATGA
19621  GATTGCCAAG GGCAATCCTT TCGCCATGGA GATCAACATC CAGGCCAACC TGTGGCGGAA
19681  CTTCCTCTAC GCGAACGTGG CGCTGTACCT GCCCGACTCC TACAAGTACA CGCCGGCCAA
19741  CATCACGCTG CCCGCCAACA CCAACACCTA CGATTACATG AACGGCCGCG TGGTAGCGCC
19801  CTCGCTGGTG GACGCCTACA TCAACATCGG GGCGCGCTGG TCGCTGGACC CCATGGACAA
19861  CGTCAACCCC TTCAACCACC ACCGCAACGC GGGCCTGCGC TACCGCTCCA TGCTCCTGGG
19921  CAACGGGCGC TACGTGCCCT TCCACATCCA GGTGCCCCAA AAGTTTTTCG CCATCAAGAG
19981  CCTCCTGCTC CTGCCCGGGT CCTACACCTA CGAGTGGAAC TTCCGCAAGG ACGTCAACAT
20041  GATCCTGCAG AGCTCCCTCG GCAACGACCT GCGCACGGAC GGGGCCTCCA TCGCCTTCAC
20101  CAGCATCAAC CTCTACGCCA CCTTCTTCCC CATGGCGCAC AACACCGCCT CCACGCTCGA
20161  GGCCATGCTG CGCAACGACA CCAACGACCA GTCCTTCAAC GACTACCTCT CGGCGGCCAA
20221  CATGCTCTAC CCCATCCCGG CCAACGCCAC CAACGTGCCC ATCTCCATCC CCTCGCGCAA
20281  CTGGGCCGCC TTCCGCGGCT GGTCCTTCAC GCGCCTCAAG ACCCGCGAGA CGCCCTCGCT
20341  CGGCTCCGGG TTCGACCCCT ACTTCGTCTA CTCGGGCTCC ATCCCCTACC TCGACGGCAC
20401  CTTCTACCTC AACCACACCT TCAAGAAGGT CTCCATCACC TTCGACTCCT CCGTCAGCTG
20461  GCCCGGCAAC GACCGCCTCC TGACGCCCAA CGAGTTCGAA ATCAAGCGCA CCGTCGACGG
20521  AGAGGGGTAC AACGTGGCCC AGTGCAACAT GACCAAGGAC TGGTTCCTGG TTCAGATGCT
20581  GGCCCACTAC AACATCGGCT ACCAGGGCTT CTACGTGCCC GAGGGCTACA AGGACCGCAT
20641  GTACTCCTTC TTCCGCAACT TCCAGCCCAT GAGCCGCCAG GTCGTGGACG AGGTCAACTA
20701  CAAGGACTAC CAGGCCGTCA CCCTGGCCTA CCAGCACAAC AACTCGGGCT TCGTCGGCTA
20761  CCTCGCGCCC ACCATGCGCC AGGGACAGCC CTACCCCGCC AACTACCCCT ACCCGCTCAT
20821  CGGCAAGAGC GCCGTCGCCA GCGTCACCCA GAAAAAGTTC CTCTGCGACC GGGTCATGTG
```

Fig. 6L

SEQ ID NO:2


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20881  GCGCATCCCC TTCTCCAGCA ACTTCATGTC CATGGGCGCG CTCACCGACC TCGGCCAGAA
20941  CATGCTCTAC GCCAACTCCG CCCACGCGCT AGACATGAAT TTCGAAGTCG ACCCCATGGA
21001  TGAGTCCACC CTTCTCTATG TTGTCTTCGA AGTCTTCGAC GTCGTCCGAG TGCACCAGCC
21061  CCACCGCGGC GTCATCGAGG CCGTCTACCT GCGCACGCCC TTCTCGGCCG GTAACGCCAC
21121  CACCTAAGCC CCGCTCTTGC TTCTTGCAAG ATGACGGCCT GTGCGGGCTC CGGCGAGCAG
21181  GAGCTCAGGG CCATCCTCCG CGACCTGGGC TGCGGGCCCT GCTTCCTGGG CACCTTCGAC
21241  AAGCGCTTCC CGGGATTCAT GGCCCCGCAC AAGCTGGCCT GCGCCATCGT CAACACGGCC
21301  GGCCGCGAGA CCGGGGGCGA GCACTGGCTG GCCTTCGCCT GGAACCCGCG CTCCCACACC
21361  TGCTACCTCT TCGACCCCTT CGGGTTCTCG AACGAGCGCC TCAAGCAGAT CTACCAGTTC
21421  GAGTACGAGG GCCTGCTGCG CCGCAGCGCC CTGGCCACCG AGGACCGCTG CGTCACCCTG
21481  GAAAAGTCCA CCCAGACCGT GCAGGGTCCG CGCTCGGCCG CCTGCGGGCT CTTCTGCTGC
21541  ATGTTCCTGC ACGCCTTCGT GCACTGGCCC GACCGCCCCA TGGACAAGAA CCCCACCATG
21601  AACTTGCTGA CGGGGGTGCC CAACGGCATG CTCCAGTCGC CCCAGGTGGA ACCCACCCTG
21661  CGCCGCAACC AGGAAGCGCT CTACCGCTTC CTCAACGCCC ACTCCGCCTA CTTTCGCTCC
21721  CACCGCGCGC GCATCGAGAA GGCCACCGCC TTCGACCGCA TGAATCAAGA CATGTAAACC
21781  GTGTGTGTAT GTGAATGCTT TATTCATAAT AAACAGCACA TGTTTATGCC ACCTTCTCTG
21841  AGGCTCTGAC TTTATTTAGA AATCGAAGGG GTTCTGCCGG CTCTCGGCAT GCCCCGCGGG
21901  CAGGGATACG TTGCGGAACT GGTACTTGGG CAGCCACTTG AACTCGGGGA TCAGCAGCTT
21961  GGGCACGGGG AGGTCGGGGA ACGAGTCGCT CCACAGCTTG CGCGTGAGTT GCAGGGCGCC
22021  CAGCAGGTCG GGCGCGGAGA TCTTGAAATC GCAGTTGGGA CCCGCGTTCT GCGCGCGAGA
22081  GTTGCGGTAC ACGGGGTTGC AGCACTGGAA CACCATCAGG GCCGGGTGCT TCACGCTCGC
22141  CAGCACCGTC GCGTCGGTGA TGCCCTCCAC GTCCAGATCC TCGGCGTTGG CCATCCCGAA
22201  GGGGGTCATC TTGCAGGTCT GCCGCCCCAT GCTGGGCACG CAGCCGGGCT TGTGGTTGCA
22261  ATCGCAGTGC AGGGGGATCA GCATCATCTG GGCCTGCTCG GAGCTCATGC CCGGGTACAT
22321  GGCCTTCATG AAAGCCTCCA GCTGGCGGAA GGCCTGCTGC GCCTTGCCGC CCTCGGTGAA
22381  GAAGACCCCG CAGGACTTGC TAGAGAACTG GTTGGTGGCG CAGCCCGCGT CGTGCACGCA
22441  GCAGCGCGCG TCGTTGTTGG CCAGCTGCAC CACGCTGCGC CCCCAGCGGT TCTGGGTGAT
22501  CTTGGCCCGG TCGGGGTTCT CCTTCAGCGC GCGCTGTCCG TTCTCGCTCG CCACATCCAT
22561  CTCGATCGTG TGCTCCTTCT GGATCATCAC GGTCCCGTGC AGGCACCGCA GCTTGCTCTC
```

Fig. 6M

SEQ ID NO:2


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22621  GGCCTCGGTG CACCCGTGCA GCCACAGCGC GCAGCCGGTG CTCTCCCAGT TCTTGTGGGC
22681  GATCTGGGAG TGCGAGTGCA CGAAGCCCTG CAGGAAGCGG CCCATCATCG CGGTCAGGGT
22741  CTTGTTGCTG GTGAAGGTCA GCGGGATGCC GCGGTGCTCC TCGTTCACAT ACAGGTGGCA
22801  GATGCGGCGG TACACCTCGC CCTGCTCGGG CATCAGCTGG AAGGCGGACT TCAGGTCGCT
22861  CTCCACGCGG TACCGGTCCA TCAGCAGCGT CATGACTTCC ATGCCCTTCT CCCAGGCCGA
22921  AACGATCGGC AGGCTCAGGG GGTTCTTCAC CGTTGTCATC TTAGTCGCCG CCGCCGAGGT
22981  CAGGGGGTCG TTCTCGTCCA GGGTCTCAAA CACTCGCTTG CCGTCCTTCT CGATGATGCG
23041  CACGGGGGGG AAGCTGAAGC CCACGGCCGC CAGCTCCTCC TCGGCCTGCC TTTCGTCCTC
23101  GCTGTCCTGG CTGATGTCTT GCAAAGGCAC ATGCTTGGTC TTGCGGGGTT TCTTTTTGGG
23161  CGGCAGAGGC GGCGGCGGAG ACGTGCTGGG CGAGCGCGAG TTCTCGCTCA CCACGACTAT
23221  TTCTTCTTCT TGGCCGTCGT CCGAGACCAC GCGGCGGTAG GCATGCCTCT TCTGGGGCAG
23281  AGGCGGAGGC GACGGGCTCT CGCGGTTCGG CGGGCGGCTG GCAGAGCCCC TTCCGCGTTC
23341  GGGGGTGCGC TCCTGGCGGC GCTGCTCTGA CTGACTTCCT CCGCGGCCGG CCATTGTGTT
23401  CTCCTAGGGA GCAACAACAA GCATGGAGAC TCAGCCATCG TCGCCAACAT CGCCATCTGC
23461  CCCCGCCGCC GACGAGAACC AGCAGAATGA AAGCTTAACC GCCCCGCCGC CCAGCCCCAC
23521  CTCCGACGCC GCGGCCCCAG ACATGCAAGA GATGGAGGAA TCCATCGAGA TTGACCTGGG
23581  CTACGTGACG CCCGCGGAGC ACGAGGAGGA GCTGGCAGCG CGCTTTTCAG CCCCGGAAGA
23641  GAACCACCAA GAGCAGCCAG AGCAGGAAGC AGAGAGCGAG CAGAACCAGG CTGGGCTCGA
23701  GCATGGCGAC TACCTGAGCG GGGCAGAGGA CGTGCTCATC AAGCATCTGA CCCGCCAATG
23761  CATCATCGTC AAGGACGCGC TGCTCGACCG CGCCGAGGTG CCCCTCAGCG TGGCGGAGCT
23821  CAGCCGCGCC TACGAGCGCA ACCTCTTCTC GCCGCGCGTG CCCCCCAAGC GCCAGCCCAA
23881  CGGCACCTGC GAGCCCAACC CGCGCCTCAA CTTCTACCCG GTCTTCGCGG TGCCCGAGGC
23941  CCTGGCCACC TACCACCTCT TTTTCAAGAA CCAAAGGATC CCCGTCTCCT GCCGCGCCAA
24001  CCGCACCCGC GCCGACGCCC TGCTCAACCT GGGCCCCGGC GCCCGCCTAC CTGATATCAC
24061  CTCCTTGGAA GAGGTTCCCA AGATCTTCGA GGGTCTGGGC AGCGACGAGA CTCGGGCCGC
24121  GAACGCTCTG CAAGGAAGCG GAGAGGAACA TGAGCACCAC AGCGCCCTGG TGGAGTTGGA
24181  AGGCGACAAC GCGCGCCTGG CGGTGCTCAA GCGCACGGTC GAGCTGACCC ACTTCGCCTA
24241  CCCGGCGCTC AACCTGCCCC CCAAGGTCAT GAGCGCCGTC ATGGACCAGG TGCTCATCAA
24301  GCGCGCCTCG CCCATTGAGG ACATGCAGGA CCCCGAGAGC TCGGACGAGG GCAAGCCCGT
```

Fig. 6N

SEQ ID NO:2


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24361  GGTCAGCGAC GAGCAGCTGG CGCGCTGGCT GGGAGCGAGT AGCACCCCCC AGAGCCTGGA
24421  AGAGCGGCGC AAGCTCATGA TGGCCGTGGT CCTGGTGACC GTGGAGCTGG AGTGTCTGCG
24481  CCGCTTCTTC GCCGACGCAG AGACCCTGCG CAAGGTCGAG GAGAACCTGC ACTACCTCTT
24541  CAGGCACGGG TTCGTGCGCC AGGCCTGCAA GATCTCCAAC GTGGAGCTGA CCAACCTGGT
24601  CTCCTACATG GGCATCCTGC ACGAGAACCG CCTGGGGCAG AACGTGCTGC ACACCACCCT
24661  GCGCGGGGAG GCCCGCCGCG ACTACATCCG CGACTGCGTC TACCTGTACC TCTGCCACAC
24721  CTGGCAGACG GGCATGGGCG TGTGGCAGCA GTGCCTGGAG GAGCAGAACC TGAAAGAGCT
24781  CTGCAAGCTC CTGCAGAAGA ACCTCAAGGC CCTGTGGACC GGGTTCGACG AGCGCACCAC
24841  CGCCTCGGAC CTGGCCGACC TCATCTTCCC CGAGCGCCTG CGGCTGACGC TGCGCAACGG
24901  GCTGCCCGAC TTTATGAGCC AAAGCATGTT GCAAAACTTT CGCTCTTTCA TCCTCGAACG
24961  CTCCGGGATC CTGCCCGCCA CCTGCTCCGC GCTGCCCTCG GACTTCGTGC CGCTGACCTT
25021  CCGCGAGTGC CCCCCGCCGC TCTGGAGCCA CTGCTACTTG CTGCGCCTGG CCAACTACCT
25081  GGCCTACCAC TCGGACGTGA TCGAGGACGT CAGCGGCGAG GGTCTGCTGG AGTGCCACTG
25141  CCGCTGCAAC CTCTGCACGC CGCACCGCTC CCTGGCCTGC AACCCCCAGC TGCTGAGCGA
25201  GACCCAGATC ATCGGCACCT TCGAGTTGCA AGGCCCCGGC GAGGAGGGCA AGGGGGGTCT
25261  GAAACTCACC CCGGGGCTGT GGACCTCGGC CTACTTGCGC AAGTTCGTGC CCGAGGACTA
25321  CCATCCCTTC GAGATCAGGT TCTACGAGGA CCAATCCCAG CCGCCCAAGG CCGAGCTGTC
25381  GGCCTGCGTC ATCACCCAGG GGGCCATCCT GGCCCAATTG CAAGCCATCC AGAAATCCCG
25441  CCAAGAATTT CTGCTGAAAA AGGGCCACGG GGTCTACTTG GACCCCCAGA CCGGAGAGGA
25501  GCTCAACCCC AGCTTCCCCC AGGATGCCCC GAGGAAGCAG CAAGAAGCTG AAAGTGGAGC
25561  TGCCGCCGCC GGAGGATTTG GAGGAAGACT GGGAGAGCAG TCAGGCAGAG GAGGAGATGG
25621  AAGACTGGGA CAGCACTCAG GCAGAGGAGG ACAGCCTGCA AGACAGTCTG GAGGAGGAAG
25681  ACGAGGTGGA GGAGGAGGAG GCAGAGGAAG AAGCAGCCGC CGCCAGACCG TCGTCCTCGG
25741  CGGAGAAAGC AAGCAGCACG GATACCATCT CCGCTCCGGG TCGGGGTCGC GGCGGCCGGG
25801  CCCACAGTAG GTGGGACGAG ACCGGGCGCT TCCCGAACCC CACCACCCAG ACCGGTAAGA
25861  AGGAGCGGCA GGGATACAAG TCCTGGCGGG GGCACAAAAA CGCCATCGTC TCCTGCTTGC
25921  AAGCCTGCGG GGGCAACATC TCCTTCACCC GGCGCTACCT GCTCTTCCAC CGCGGGGTGA
25981  ACTTCCCCCG CAACATCTTG CATTACTACC GTCACCTCCA CAGCCCCTAC TACTGTTTCC
26041  AAGAAGAGGC AGAAACCCAG CAGCAGCAGA AAACCAGCGA CAGCGGCAGC AGCTAGAAAA
```

Fig. 60

SEQ ID NO:2


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26101  TCCACAGCGG CAGGTGGACT GAGGATCGCG GCGAACGAGC CGGCGCAGAC CCGGGAGCTG
26161  AGGAACCGGA TCTTTCCCAC CCTCTATGCC ATCTTCCAGC AGAGTCGGGG GCAGGAGCAG
26221  GAACTGAAAG TCAAGAACCG TTCTCTGCGC TCGCTCACCC GCAGTTGTCT GTATCACAAG
26281  AGCGAAGACC AACTTCAGCG CACTCTCGAG GACGCCGAGG CTCTCTTCAA CAAGTACTGC
26341  GCGCTCACTC TTAAAGAGTA GCCCGCGCCC GCCCACACAC GGAAAAAGGC GGGAATTACG
26401  TCACCACCTG CGCCCTTCGC CCGACCATCA TCATGAGCAA AGAGATTCCC ACGCCTTACA
26461  TGTGGAGCTA CCAGCCCCAG ATGGGTCTGG CCGCCGGCGC CGCCCAGGAC TACTCCACCC
26521  GCATGAACTG GCTCAGTGCC GGGCCCGCGA TGATCTCACG GGTGAATGAC ATCCGCGCCC
26581  ATCGAAACCA GATACTCCTA GAACAGTCAG CGATCACCGC CACGCCCCGC CATCACCTTA
26641  ATCCGCGTAA TTGGCCCGCC GCCCTGGTGT ACCAGGAAAT TCCCCAGCCC ACGACCGTAC
26701  TACTTCCGCG AGACGCCCAG GCCGAAGTCC AGCTGACTAA CTCAGGTGTC CAGCTGGCCG
26761  GCGGCGCCGC CCTGTGTCGT CACCGCCCCG CTCAGGGTAT AAAGCGGCTG GTGATCCGAG
26821  GCAGAGGCAC ACAGCTCAAC GACGAGGTGG TGAGCTCTTC GCTGGGTCTG CGACCTGACG
26881  GAGTCTTCCA ACTCGCCGGA TCGGGGAGAT CTTCCTTCAC GCCTCGTCAG GCCGTCCTGA
26941  CTTTGGAGAG TTCGTCCTCG CAGCCCCGCT CGGGCGGCAT CGGCACTCTC CAGTTCGTGG
27001  AGGAGTTCAC TCCCTCGGTC TACTTCAACC CCTTCTCCGG CTCCCCCGGC CACTACCCGG
27061  ACGAGTTCAT CCCGAACTTC GACGCCATCA GCGAGTCGGT GGACGGCTAC GATTGAATGT
27121  CCCATGGTGG CGCAGCTGAC CTAGCTCGGC TTCGACACCT GGACCACTGC CGCCGCTTCC
27181  GCTGCTTCGC TCGGGATCTC GCCGAGTTTG CCTACTTTGA GCTGCCCGAG GAGCACCCTC
27241  AGGGCCCGGC CCACGGAGTG CGGATCATCA TCGAAGGGGG CCTCGACTCC CACCTGCTTC
27301  GGATCTTCAG CCAGCGACCG ATCCTGGTCG AGCGCGAGCA AGGACAGACC CGTCTGACCC
27361  TGTACTGCAT CTGCAACCAC CCCGGCCTGC ATGAAAGTCT TTGTTGTCTG CTGTGTACTG
27421  AGTATAATAA AAGCTGAGAT CAGCGACTAC TCCGGACTCG ATTGTGGTGT TCCTGCTATC
27481  AACCGGTCCC TGTTCTTCAC CGGGAACGAG ACCGAGCTCC AGCTCCAGTG TAAGCCCCAC
27541  AAGAAGTACC TCACCTGGCT GTTCCAGGGC TCTCCGATCG CCGTTGTCAA CCACTGCGAC
27601  AACGACGGAG TCCTGCTGAG CGGCCCTGCC AACCTTACTT TTTCCACCCG CAGAAGCAAG
27661  CTCCAGCTCT TCCAACCCTT CCTCCCCGGG ACCTATCAGT GCGTCTCGGG ACCCTGCCAT
27721  CACACCTTCC ACCTGATCCC GAATACCACA GCGCCGCTCC CCGCTACTAA CAACCAAACT
27781  ACCCACCAAC GCCACCGTCG CGACCTTTCC TCTGAATCTA ATACTACCAC CCACACCGGA
```

Fig. 6P

SEQ ID NO:2


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27841  GGTGAGCTCC GAGGTCGACC AACCTCTGGG ATTTACTACG GCCCCTGGGA GGTGGTGGGG
27901  TTAATAGCGC TAGGCCTAGT TGTGGGTGGG CTTTTGGCTC TCTGCTACCT ATACCTCCCT
27961  TGCTGTTCGT ACTTAGTGGT GCTGTGTTGC TGGTTTAAGA AATGGGGAAG ATCACCCTAG
28021  TGAGCTGCGG TGTGCTGGTG GCGGTGTTGC TTTCGATTGT GGGACTGGGC GGCGCGGCTG
28081  TAGTGAAGGA GGAGAAGGCC GATCCCTGCT TGCATTTCAA TCCCGACAAA TGCCAGCTGA
28141  GTTTTCAGCC CGATGGCAAT CGGTGCACGG TGCTGATCAA GTGCGGATGG GAATGTGAGA
28201  ACGTGAGAAT CGAGTACAAT AACAAGACTC GGAACAATAC TCTCGCGTCC GTGTGGCAAC
28261  CCGGGGACCC CGAGTGGTAC ACCGTCTCTG TCCCCGGTGC TGACGGCTCC CCGCGCACCG
28321  TGAATAATAC TTTCATTTTT GCGCACATGT GCGACACGGT CATGTGGATG AGCAAGCAGT
28381  ACGATATGTG GCCCCCCACG AAGGAGAACA TCGTGGTCTT CTCCATCGCT TACAGCGTGT
28441  GCACGGCGCT AATCACCGCT ATCGTGTGCC TGAGCATTCA CATGCTCATC GCTATTCGCC
28501  CCAGAAATAA TGCCGAAAAA GAGAAACAGC CATAACACGT TTTTTCACAC ACCTTTTTCA
28561  GACCATGGCC TCTGTTACTG CCCTAATTAT TTTTTTGGGT CTCGTGGGCA CTAGCAGCAC
28621  TTTTCAGCAT ATAAACAAAA CTGTTTATGC TGGTTCTAAT TCTGTATTAC CTGGGCATCA
28681  ATCACACCAG AAAGTTTCAT GGTACTGGTA TGATAAAAAT AACACGCCAG TCACACTCTG
28741  CAAGGGTCAT CAAACACCCA TAAACCGTAG TGGAATTTTT TTTAAATGTA ATCATAATAA
28801  TATTACACTA CTTTCAATTA CAAAGCACTA TTCTGGTACT TACTATGGAA CCAATTTTAA
28861  CATAAAACAG GACACTTACT ATAGTGTCAC AGTATTGGAT CCAACTACTC CTAGAACAAC
28921  TACAAAACCC ACAACTACTA AGAGGCACAC TAAACCTAAA ACTACCAAGA AAACCACTGT
28981  CAAAACAACA ACTAGGACCA CCACAACTAC AGAGGCTACC ACCAGCACAA CACTTGCTGC
29041  AACTACACAC ACACACACTG AGCTAACCTT ACAGACCACT AATGATTTGA TAGCCCTGTT
29101  GCAAAAGGGG GATAACAGCA CCACTTCCGA TGAGGAAATA CCCAAATCCA TGATTGGCAT
29161  TATTGTTGCT GTAGTGGTGT GCATGTTGAT CATCGCCTTG TGCATGGTGT ACTATGCCTT
29221  CTGCTACAGA AAGCACAGAC TGAACGACAA GCTGGAACAC TTACTAAGTG TTGAATTTTA
29281  ATTTTTTAGA ACCATGAAGA TCCTAGGCCT TTTAGTTTTT TCTATCATTA CCTCTGCTCT
29341  TTGTGAATCA GTGAATAAAG ATGTTACTAT TACCACTGGT TCTAATTATA CACTGAAAGG
29401  GCCACCCTCA GGTATGCTTT CGTGGTATTG CTATTTTGGA ACTGACACTG ATCAAACTGA
29461  ATTATGCAAT TTTCAAAAAG GCAAAACCTC AAACTCTAAA ATCTCTAATT ATCAATGCAA
29521  TGGCACTGAT CTGATACTAC TCAATGTCAC GAAAGCATAT GGTGGCAGTT ATTCTTGCCC
```

Fig. 6Q

SEQ ID NO:2


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29581  TGGACAAAAC ACTGAAGAAA TGATTTTTTA CAAAGTGGAA GTGGTTGATC CCACTACTCC
29641  ACCCACCACC ACAACTACTC ACACCACACA CACAGAACAA ACCACAGCAG AGGAGGCAGC
29701  AAAGTTAGCC TTGCAGGTCC AAGACAGTTC ATTTGTTGGC ATTACCCCTA CACCTGATCA
29761  GCGGTGTCCG GGGCTGCTAG TCAGCGGCAT TGTCGGTGTG CTTTCGGGAT TAGCAGTCAT
29821  AATCATCTGC ATGTTCATTT TTGCTTGCTG CTATAGAAGG CTTTACCGAC AAAAATCAGA
29881  CCCACTGCTG AACCTCTATG TTTAATTTTT TCCAGAGCCA TGAAGGCAGT TAGCACTCTA
29941  GTTTTTTGTT CTTTGATTGG CATTGTTTTT AGTGCTGGGT TTTTGAAAAA TCTTACCATT
30001  TATGAAGGTG AGAATGCCAC TCTAGTGGGC ATCAGTGGTC AAAATGTCAG CTGGCTAAAA
30061  TACCATCTAG ATGGGTGGAA AGACATTTGC GATTGGAATG TCACTGTGTA TACATGTAAT
30121  GGAGTTAACC TCACCATTAC TAATGCCACC CAAGATCAGA ATGGTAGGTT TAAGGGTCAG
30181  AGTTTCACTA GAAATAATGG GTATGAATCC CATAACATGT TTATCTATGA CGTCACTGTC
30241  ATCAGAAATG AGACCGCCAC CACCACACAG ATGCCCACTA CACACAGTTC TACCACTACT
30301  ACCAAGCAAA CCACACAGAC AACCACTTTT TATACATCAA CTCAGCATAT GACCACCACT
30361  ACAGCAGCAA AGCCAAGTAG CGCAGCGCCT CAGCCACAGG CTTTGGCTTT GAAAGCTGCA
30421  CAACCTAGTA CAACTACTAA GACCAATGAG CAGACTACTG ATTTTTTGTC CACTGTCGAG
30481  AGCCACACCA CAGCTACCTC CAGTGCCTTC TCTAGCACCG CCAATCTCTC CTCGCTTTCC
30541  TCTACACCAA TCAGTCCCGC TACTACTCCT AGCCCCGCTC CTCTTCCCAC TCCCCTGAAG
30601  CAAACAGACG GCGGCATGCA ATGGCAGATC ACCCTGCTCA TTGTGATCGG GTTGGTCATC
30661  CTGGCCGTGT TGCTCTACTA CATCTTCTGC CGCCGCATTC CCAACGCGCA CCGCAAGCCG
30721  GTCTACAAGC CCATCGTTGT CGGGCAGCCG GAGCCGCTTC AGGTGGAAGG GGGTCTAAGG
30781  AATCTTCTCT TCTCTTTTAC AGTATGGTGA TTGAACTATG ATTCCTAGAC AATTCTTGAT
30841  CACTATTCTT ATCTGCCTCC TCCAAGTCTG TGCCACCCTC GCTCTGGTGG CCAACGCCAG
30901  TCCAGACTGT ATTGGGCCCT TCGCCTCCTA CGTGCTCTTT GCCTTCATCA CCTGCATCTG
30961  CTGTTGTAGC ATAGTCTGCC TGCTTATCAC CTTCTTCCAG TTCATTGACT GGATCTTTGT
31021  GCGCATCGCC TACCTGCGCC ACCACCCCCA GTACCGCGAC CAGCGAGTGG CGCGACTGCT
31081  CAGGCTCCTC TGATAAGCAT GCGGGCTCTG CTACTTCTCG CGCTTCTGCT GTTAGTGCTC
31141  CCCCGTCCCG TCGACCCCCG GTCCCCCGAG GAGGTCCGCA AATGCAAATT CCAAGAACCC
31201  TGGAAATTCC TCAAATGCTA CCGCCAAAAA TCAGACATGC ATCCCAGCTG GATCATGATC
31261  ATTGGGATCG TGAACATTCT GGCCTGCACC CTCATCTCCT TTGTGATTTA CCCCTGCTTT
```

Fig. 6R

SEQ ID NO:2


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31321  GACTTTGGTT GGAACTCGCC AGAGGCACTC TATCTCCCGC CTGAGCCTGA CACACCACCA
31381  CAGCAGCAAC CTCAGGCACA CGCACTACCA CCACCACAGC CTAGGCCACA ATACATGCCC
31441  ATATTAGACT ATGAGGCCGA GCCACAGCGA CCCATGCTCC CCGCTATTAG TTACTTCAAT
31501  CTAACCGGCG GAGATGACTG ACCCACTGGC CAACAACAAC GTCAACGACC TTCTCCTGGA
31561  CATGGACGGC CGCGCCTCGG AGCAGCGACT CGCCCAACTC CGCATCCGCC AGCAGCAGGA
31621  GAGAGCCGTC AAGGAGCTGC AGGATGCGGT GGCCATCCAC CAGTGCAAGA AAGGCATCTT
31681  CTGCCTGGTG AAGCAGGCCA AGATCTCCTA CGAGGTCACC CAGACCGACC ATCGCCTCTC
31741  CTACGAGCTC CTGCAGCAGC GCCAGAAGTT CACCTGCCTG GTCGGAGTCA ACCCCATCGT
31801  CATCACCCAG CAGTCGGGCG ATACCAAGGG GTGCATCCAC TGCTCCTGCG ACTCCCCCGA
31861  GTGCGTTCAC ACCATGATCA AGACCCTCTG CGGCCTCCGC GACCTCCTCC CCATGAACTA
31921  ATCACCCCCT TATCCAGTGA AATAAAGATC ATATTGATGA TGATTTAAAT AAAAAAATAA
31981  TCATTTGATT TGAAATAAAG ATACAATCAT ATTGATGATT TGAGTTTAAC AAAAATAAAG
32041  AATCACTTAC TTGAAATCTG ATACCAGGTC TCTGTCCATG TTTTCTGCCA ACACCACCTC
32101  ACTCCCCTCT TCCCAGCTCT GGTACTGCAG GCCCCGGCGG GCTGCAAACT TCCTCCACAC
32161  GCTGAAGGGG ATGTCAAATT CCTCCTGTCC CTCAATCTTC ATTTTCTCTT CTATCAGATG
32221  TCCAAAAAGC GCGCGCGGGT GGATGATGAC TTCGACCCCG TGTACCCCTA CGATGCAGAC
32281  AACGCACCGA CTGTGCCCTT CATCAACCCT CCCTTCGTCT CTTCAGATGG ATTCCAAGAA
32341  AAGCCCCTGG GGGTGTTGTC CCTGCGACTG GCCGATCCCG TCACCACCAA GAACGGGGCT
32401  GTCACCCTCA AGCTGGGGGA GGGGGTGGAC CTCGACGACT CGGGAAAACT CATCTCCAAA
32461  AATGCCACCA AGGCCACTGC CCCTCTCAGT ATTTCCAACA ACACCATTTC CCTTAACATG
32521  GATACCCCTC TTTACAACAA CAATGGAAAG CTAGGTATGA AGGTAACCGC ACCATTAAAG
32581  ATATTAGACA CAGATCTACT AAAAACACTT GTTGTTGCTT ATGGGCAGGG ATTAGGAACA
32641  AACACCAATG GTGCTCTTGT TGCCCAACTA GCATACCCAC TTGTTTTTAA TACCGCTAGC
32701  AAAATTGCCC TTAATTTAGG CAATGGACCA TTAAAAGTGG ATGCAAATAG ACTGAACATT
32761  AATTGCAAAA GAGGTATCTA TGTCACTACC ACAAAAGATG CACTGGAGAT TAATATCAGT
32821  TGGGCAAATG CTATGACATT TATAGGAAAT GCCATTGGTG TCAATATTGA CACAAAAAAA
32881  GGCCTACAGT TCGGCACTTC AAGCACTGAA ACAGATGTTA AAAATGCTTT TCCACTCCAA
32941  GTAAAACTTG GAGCTGGTCT TACATTTGAC AGCACAGGTG CCATTGTTGC TTGGAACAAA
33001  GAAGATGACA AACTTACACT GTGGACCACA GCCGATCCAT CTCCAAACTG TCACATATAT
```

Fig. 6S

SEQ ID NO:2


```
33061  TCTGCAAAGG ATGCTAAGCT TACACTCTGC TTGACAAAGT GTGGTAGTCA GATACTGGGC
33121  ACTGTTTCTC TCATAGCTGT TGATACTGGT AGCTTAAATC CAATAACAGG AAAAGTAACC
33181  ACTGCTCTTG TTTCACTTAA ATTCGATGCC AATGGAGTTT TGCAAGCCAG TTCAACACTA
33241  GATAAAGAAT ATTGGAATTT CAGAAAAGGA GATGTGACAC CTGCTGACCC CTACACTAAT
33301  GCTATAGGCT TTATGCCCAA CCTTAATGCA TACCCAAAAA ACACAAACGC AGCTGCAAAA
33361  AGTCACATTG TTGGAAAAGT ATACCTACAT GGGGATGAAA GCAAGCCACT AGACTTGATA
33421  ATTACATTTA ATGAAACCAG TGATGAATCC TGTACTTATT GCATTAACTT TCAGTGGCAG
33481  TGGGGAACTG ACCAATATAA AGATGAAACA CTTGCAGTCA GTTCATTCAC CTTCTCATAC
33541  ATTGCTAAAG AATAACATCC ACCCTGCATG CCAACCCATT TCCCTCTATC TATACATGGA
33601  AAACTCTGAA GCAGAAAAAA TAAAGTTCAA GTGTTTTATT GATTCAACAG TTTTTACAGA
33661  ATTCGAGTAG TTATTTTCCC TCCACCCTCC CAACTCATGG AATACACCAT CCTCTCCCCA
33721  CGCACAGCCT TAAACATCTG AATGCCATTG GTAATGGACA TGGTTTTGGC CTCCACATTC
33781  CACACAGTTT CAGAGCGAGC CAGTCTCGGG TCGGTCAGGG AGATGAAACC CTCCGGGCAC
33841  TCCTGCATCT GCACCTCACA GTTCAACAGC TGAGGGCTGT CCTCGGTGGT CGGGATCACA
33901  GTTATCTGGA AGAAGAGCGA TGAGAGTCAT AATCCGCGAA CGGGATCGGG CGGTTGTGGC
33961  GCATCAGGCC CCGCAGCAGT CGCTGTCTGC GCCGCTCCGT CAAGCTGCTG CTCAAGGGGT
34021  CCGGGTCCAG GGACTCCCCG CGCATGATGC CGATGGCCCT GAGCATCAGT CGCCTGGTGC
34081  GGCGGGCGCA GCAGCGGATG CGGATCTCAC TCAGGTCGGA ACAGTACGTG CAGCACAGCA
34141  CTACCAAGTT GTTCAACAGT CCATAGTTCA ACGTGCTCCA GCCAAAACTC ATCTGTGGAA
34201  CTATGCTGCC CACATGTCCA TCGTACCAGA TCCTGATGTA AATCAGGTGG CGCCCCCTCC
34261  AGAACACACT GCCCATGTAC ATGATCTCCT TGGGCATGTG CAGGTTCACC ACCTCCCGGT
34321  ACCACATCAC CCGCTGGTTG AACATGCAGC CCCGGATGAT CCTGCGGAAC CACAGGGCCA
34381  GCACCGCCCC GCCCGCCATG CAGCGCAGGG ACCCCGGGTC CTGGCAATGG CAGTGGATGA
34441  TCCACCGCTC GTACCCGTGG ATCATCTGGG AGCTGAACAA GTCTATGTTG GCACAGCACA
34501  GGCACACGCT CATGCATCTC TTCAGCACTC TCAGCTCCTC GGGGGTCAAA ACCATATCCC
34561  AGGGTACGGG GAACTCTTGC AGGACAGCGA ACCCCGCAGA ACAGGGCAAA CCTCGCACAG
34621  AACTTACATT GTGCATGGAC AGGGTATCGC AATCAGGCAG CACCGGGTGA TCCTCCACCA
34681  GGGAAGCGCG GGTCTCGATT TCCTCACAGC GTGGTAAGGG GGCCGGTCGA TACGGGTGAT
34741  GGCGGGACGC GGCTGATCGT GTTCGCGATC GTGTCATGAT GCAGTTGCTT TCGGACATTT
```

Fig. 6T

SEQ ID NO:2


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34801  TCGTACTTGC TATAGCAGAA CCTGGTCCGG GCGCTGCACA CCGATCGCCG GCGGCGGTCT
34861  CGGCGCTTGG AACGCTCCGT GTTGAAATTG TAAAACAGCC ACTCTCTCAG ACCGTGCAGC
34921  AGATCTAGGG CCTCAGGAGT GATGAAGATC CCATCATGCC TGATGGCTCT GATCACATCG
34981  ACCACCGTGG AATGGGCCAG ACCCAGCCAG ATGATGCAAT TTTGTTGGGT TTCGGTGACG
35041  GCGGGGGAGG GAAGAACAGG AAGAACCATG ATTAACTTTA ATCCAAACGG TCTCGGAGCA
35101  CTTCAAAATG AAGGTCGCGG AGATGGCACC TCTCGCCCCC GCTGTGTTGG TGGAAAATAA
35161  CAGCCAGGTC AAAGGTGATA CGGTTCTCGA GATGTTCCAC GGTGGCTTCC AGCAAAGCCT
35221  CCACGCGCAC ATCCAGAAAC AAGACAATAG CGAAAGCGGG AGGGTTCTCT AATTCCTCAA
35281  TCATCATGTT ACACTCCTGC ACCATCCCCA GATAATTTTC ATTTTTCCAG CCTTGAATGA
35341  TTCGAACTAG TTCCTGAGGT AAATCCAAGC CAGCCATGAT AAAGAGCTCG CGCAGAGCGC
35401  CCTCCACCGG CATTCTTAAG CACACCCTCA TAATTCCAAG ATATTCTGCT CCTGGTTCAC
35461  CTGCAGCAGA TTGACAAGCG GAATATCAAA CTCTCTGCCG CGATCCCTAA GCTCCTCCCT
35521  CAGCAATAAC TGTAAGTACT CTCTCATATC CTCTCCGAAA TTTTTAGCCA TAGGACCGCC
35581  AGGAATAAGA TTAGGGCAAG CCACAGTACA GATAAACCGA AGTCCTCCCC AGTGAGCATT
35641  GCCAAATGCA AGACTGCTAT AAGCATGCTG GCTAGACCCG GTGATATCTT CCAGATAATT
35701  GGACAGAAAA TCGCCCAGGC AATTTTTAAG AAAATCAACA AAAGAAAAAT CCTCCAGGTG
35761  CACGTTTAGA GCCTCGGGAA CAACGATGGA GTAAATGCAA GCGGTGCGTT CCAGCATGGT
35821  TAGTTAGCTG ATCTGTAGAA AAAACAAAAA TGAACATTAA ACCATGCTAG CCTGGCGAAC
35881  AGGTGGGTAA ATCGTTCTTT CCAGCACCAG GCAGGCCACG GGGTCTCCGG CGCGACCCTC
35941  GTAAAAATTG TCGCTATGAT TGAAAACCAT CACAGAGAGA CGTTCCCGGT GGCCGGCGTG
36001  AATGATTCGA CAAGACGAAT ACACCCCCGG AACATTGGCG TCCGCGAGTG AAAAAAAGCG
36061  CCCGAGGAAG CAATAAGGCA CTACAATGCT CAGTCTCAAG TCCAGCAAAG CGATGCCATG
36121  CGGATGAAGC ACAAAATTCT CAGGTGCGTA CAAAATGTAA TTACTCCCCT CCTGCACAGG
36181  CAGCAAAGCC CCCGATCCCT CCAGGTACAC ATACAAAGCC TCAGCGTCCA TAGCTTACCG
36241  AGCAGCAGCG GCACACAACA GGCGCAAAAG TCAGAGAAAG GCTGAGAGCT CTAACCTGTC
36301  CACCCGCTCT CTGCTCAATA TATAGCCCAG ATCTACACTG ACGTAAAGGC CAAAGTCTAA
36361  AAATACCCGC CAAATAATCA CACACGCCCA GCACACGCCC AGAAACCGGT GACACACTCA
36421  GAAAAATACG CGCACTTCCT CAAACGCCCA AACTGCCGTC ATTTCCGGGT TCCCACGCTA
36481  CGTCATCAAA ATTCAACTTT CAAATTCCGT CGACCGTTAA AAACGTCACC CGCCCCGCCC
```

Fig. 6U

SEQ ID NO:2

36541 CTAACGGTCG CCGCTCCCGC AGCCAATCAG CGCCCCGCAT CCCCAAATTC AAACGGCTCA

36601 TTTGCATATT AACGCGCACC AAAAGTTTGA GGTATATTAT TGATGATG

Fig. 6V

SEQ ID NO:3


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   1 CATCATCAAT AATATACCTC AAACTTTTGG TGCGCGTTAA TATGCAAATG AGCTGTTTGA
  61 ATTTGGGGAG GGAGGAAGGT GATTGGCTGC GGGAGCGGCG ACCGTTAGGG GCGGGGCGGG
 121 TGACGTTTTG ATGACGTGGC TATGAGGCGG AGCCGGTTTG CAAGTTCTCG TGGGAAAAGT
 181 GACGTCAAAC GAGGTGTGGT TTGAACACGG AAATACTCAA TTTTCCCGCG CTCTCTGACA
 241 GGAAATGAGG TGTTTCTGGG CGGATGCAAG TGAAAACGGG CCATTTTCGC GCGAAAACTG
 301 AATGAGGAAG TGAAAATCTG AGTAATTTCG CGTTTATGGC AGGGAGGAGT ATTTGCCGAG
 361 GGCCGAGTAG ACTTTGACCG ATTACGTGGG GGTTTCGATT ACCGTATTTT TCACCTAAAT
 421 TTCCGCGTAC GGTGTCAAAG TCCGGTGTTT TTACGTAGGC GTCAGCTGAT CGCCAGGGTA
 481 TTTAAACCTG CGCTCTCTAG TCAAGAGGCC ACTCTTGAGT GCCAGCGAGT AGAGTTTTCT
 541 CCTCCGCGCC GCGAGTCAGA TCTACACTTT GAAAGATGAG GCACCTGAGA GACCTGCCCG
 601 GTAATGTTTT CCTGGCTACT GGGAACGAGA TTCTGGAATT GGTGGTGGAC GCCATGATGG
 661 GTGACGACCC TCCAGAGCCC CCTACCCCAT TTGAGGCGCC TTCGCTGTAC GATTTGTATG
 721 ATCTGGAGGT GGATGTGCCC GAGAGCGACC CTAACGAGGA GGCGGTGAAT GATTTGTTTA
 781 GCGATGCCGC GCTGCTGGCT GCCGAGCAGG CTAATACGGA CTCTGGCTCA GACAGCGATT
 841 CCTCTCTCCA TACCCCGAGA CCCGGCAGAG GTGAGAAAAA GATCCCCGAG CTTAAAGGGG
 901 AAGAGCTCGA CCTGCGCTGC TATGAGGAAT GCTTGCCTCC GAGCGATGAT GAGGAGGACG
 961 AGGAGGCGAT TCGAGCTGCG GTGAACCAGG GAGTGAAAAC TGCGGGCGAG AGCTTTAGCC
1021 TGGACTGTCC TACTCTGCCC GGACACGGCT GTAAGTCTTG TGAATTTCAT CGCATGAATA
1081 CTGGAGATAA GAATGTGATG TGTGCCCTGT GCTATATGAG AGCTTACAAC CATTGTGTTT
1141 ACAGTAAGTG TGATTAACTT TAGTTGGGAA GGCAGAGGGT GACTGGGTGC TGACTGGTTT
1201 ATTTATGTAT ATGTTTTTTT ATGTGTAGGT CCCGTCTCTG ACGTAGATGA GACCCCCACT
1261 TCAGAGTGCA TTTCATCACC CCCAGAAATT GGCGAGGAAC CGCCCGAAGA TATTATTCAT
1321 AGACCAGTTG CAGTGAGAGT CACCGGGCGG AGAGCAGCTG TGGAGAGTTT GGATGACTTG
1381 CTACAGGGTG GGGATGAACC TTTGGACTTG TGTACCCGGA AACGCCCCAG GCACTAAGTG
1441 CCACACATGT GTGTTTACTT AAGGTGATGT CAGTATTTAT AGGGTGTGGA GTGCAATAAA
1501 ATCCGTGTTG ACTTTAAGTG CGTGTTTTAT GACTCAGGGG TGGGGACTGT GGGTATATAA
1561 GCAGGTGCAG ACCTGTGTGG TCAGTTCAGA GCAGGACTCA TGGAGATCTG GACTGTCTTG
1621 GAAGACTTTC ACCAGACTAG ACAGTTGCTA GAGAACTCAT CGGAGGGAGT CTCTTACCTG
1681 TGGAGATTCT GCTTCGGTGG GCCTCTAGCT AAGCTAGTCT ATAGGGCCAA ACAGGATTAT
1741 AAGGAACAAT TTGAGGATAT TTTGAGAGAG TGTCCTGGTA TTTTTGACTC TCTCAACTTG
1801 GGCCATCAGT CTCACTTTAA CCAGAGTATT CTGAGAGCCC TTGACTTTTC TACTCCTGGC
1861 AGAACTACCG CCGCGGTAGC CTTTTTTGCC TTTATTCTTG ACAAATGGAG TCAAGAAACC
1921 CATTTCAGCA GGGATTACCG TCTGGACTGC TTAGCAGTAG CTTTGTGGAG AACATGGAGG
1981 TGCCAGCGCC TGAATGCAAT CTCCGGCTAC TTGCCAGTAC AGCCGGTAGA CACGCTGAGG
2041 ATCCTGAGTC TCCAGTCACC CCAGGAACAC CAACGCCGCC AGCAGCCGCA GCAGGAGCAG
2101 CAGCAAGAGG AGGACCGAGA AGAGAACCCG AGAGCCGGTC TGGACCCTCC GGTGGCGGAG
2161 GAGGAGGAGT AGCTGACTTG TTTCCCGAGC TGCGCCGGGT GCTGACTAGG TCTTCCAGTG
2221 GACGGGAGAG GGGGATTAAG CGGGAGAGGC ATGAGGAGAC TAGCCACAGA ACTGAACTGA
2281 CTGTCAGTCT GATGAGCCGC AGGCGCCCAG AATCGGTGTG GTGGCATGAG GTGCAGTCGC
2341 AGGGGATAGA TGAGGTCTCG GTGATGCATG AGAAATATTC CCTAGAACAA GTCAAGACTT
2401 GTTGGTTGGA GCCCGAGGAT GATTGGGAGG TAGCCATCAG GAATTATGCC AAGCTGGCTC
2461 TGAAGCCAGA CAAGAAGTAC AAGATTACCA AACTGATTAA TATCAGAAAT TCCTGCTACA
2521 TTTCAGGGAA TGGGGCCGAG GTGGAGATCA GTACCCAGGA GAGGGTGGCC TTCAGATGTT
2581 GTATGATGAA TATGTACCCG GGGGTGGTGG GCATGGAGGG AGTCACCTTT ATGAACACGA
2641 GGTTCAGGGG TGATGGGTAT AATGGGGTGG TCTTTATGGC CAACACCAAG CTGACAGTGC
2701 ACGGATGCTC CTTCTTTGGC TTCAATAACA TGTGCATCGA GGCCTGGGGC AGTGTTTCAG
2761 TGAGGGGATG CAGCTTTTCA GCCAACTGGA TGGGGGTCGT GGGCAGAACC AAGAGCAAGG
2821 TGTCAGTGAA GAAATGCCTG TTCGAGAGGT GCCACCTGGG GGTGATGAGC GAGGGCGAAG
2881 CCAAAGTCAA ACACTGCGCC TCTACCGAGA CGGGCTGCTT TGTGCTGATC AAGGGCAATG
2941 CCCAAGTCAA GCATAACATG ATCTGTGGGG CCTCGGATGA GCGCGGCTAC CAGATGCTGA
3001 CCTGCGCCGG TGGGAACAGC CATATGCTGG CCACCGTGCA TGTGGCCTCG CACCCCCGCA
3061 AGACATGGCC CGAGTTCGAG CACAACGTCA TGACCCGCTG CAATGTGCAC CTGGGCTCCC
3121 GCCGAGGCAT GTTCATGCCC TACCAGTGCA ACATGCAATT TGTGAAGGTG CTGCTGGAGC
3181 CCGATGCCAT GTCCAGAGTG AGCCTGACGG GGGTGTTTGA CATGAATGTG GAGCTGTGGA
3241 AAATTCTGAG ATATGATGAA TCCAAGACCA GGTGCCGGGC CTGCGAATGC GGAGGCAAGC
3301 ACGCCAGGCT TCAGCCCGTG TGTGTGGAGG TGACGGAGGA CCTGCGACCC GATCATTTGG
3361 TGTTGTCCTG CAACGGGACG GAGTTCGGCT CCAGCGGGGA AGAATCTGAC TAGAGTGAGT
3421 AGTGTTTGGG GCTGGGTGTG AGCCTGCATG AGGGGCAGAA TGACTAAAAT CTGTGGTTTT
3481 CTGTGTGTTG CAGCAGCATG AGCGGAAGCG CCTCCTTTGA GGGAGGGGTA TTCAGCCCTT
3541 ATCTGACGGG GCGTCTCCCC TCCTGGGCGG GAGTGTGTCA GAATGTTATG GNATCCACGG
3601 TGGACGGCCG GCCCGTGCAG CCCGCGAACT CTTCAACCCT GACCTACGCG ACCCTGAGCT
```

Fig. 7A

SEQ ID NO: 3


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3661 CCTCGTCCGT GGACGCAGCT GCCGCCGCAG CTGCTGCTTC CGCCGCCAGC GCCGTGCGCG
3721 GAATGGCCCT GGGCGCCGGC TACTACAGCT CTCTGGTGGC CAACTCGAGT TCCACCAATA
3781 ATCCCGCCAG CCTGAACGAG GAGAAGCTGC TGCTGCTGAT GGCCCAGCTC GAGGCCCTGA
3841 CCCAGCGCCT GGGCGAGCTG ACCCAGCAGG TGGCTCAGCT GCAGGCGGAG ACGCGGGCCG
3901 CGGTTGCCAC GGTGAAAACC AAATAAAAAA TGAATCAATA AATAAACGGA GACGGTTGTT
3961 GATTTTAACA CAGAGTCTTG AATCTTTATT TGATTTTTCG CGCGCGGTAG GCCCTGGACC
4021 ACCGGTCTCG ATCATTGAGC ACCCGGTGGA TCTTTTCCAG GACCCGGTAG AGGTGGGCTT
4081 GGATGTTGAG GTACATGGGC ATGAGCCCGT CCCGGGGGTG GAGGTAGCTC CATTGCAGGG
4141 CCTCGTGCTC GGGGATGGTG TTGTAAATCA CCCAGTCATA GCAGGGGCGC AGGGCGTGGT
4201 GCTGCACGAT GTCCTTGAGG AGGAGACTGA TGGCCACGGG CAGCCCCTTG GTGTAGGTGT
4261 TGACGAACCT GTTGAGCTGG GAGGGATGCA TGCGGGGGGA GATGAGATGC ATCTTGGCCT
4321 GGATCTTGAG ATTGGCGATG TTCCCGCCCA GATCCCGCCG GGGGTTCATG TTGTGCAGGA
4381 CCACCAGCAC GGTGTATCCG GTGCACTTGG GGAATTTGTC ATGCAACTTG GAAGGGAAGG
4441 CGTGAAAGAA TTTGGAGACG CCCTTGTGAC CGCCCAGGTT TTCCATGCAC TCATCCATGA
4501 TGATGGCGAT GGGCCCGTGG GCGGCGGCCT GGGCAAAGAC GTTTCGGGGG TCGGACACAT
4561 CGTAGTTGTG GTCCTGGGTG AGCTCGTCAT AGGCCATTTT AATGAATTTG GGGCGGAGGG
4621 TGCCCGACTG GGGGACGAAG GTGCCCTCGA TCCCGGGGGC GTAGTTGCCC TCGCAGATCT
4681 GCATCTCCCA GGCCTTGAGC TCGGAGGGGG GGATCATGTC CACCTGCGGG GCGATGAAAA
4741 AAACGGTTTC CGGGGCGGGG GAGATGAGCT GGGCCGAAAG CAGGTTCCGG AGCAGCTGGG
4801 ACTTGCCGCA ACCGGTGGGG CCGTAGATGA CCCCGATGAC CGGCTGCAGG TGGTAGTTGA
4861 GGGAGAGACA GCTGCCGTCC TCGCGGAGGA GGGGGGCCAC CTCGTTCATC ATCTCGCGCA
4921 CATGCATGTT CTCGCGCACG AGTTCCGCCA GGAGGCGCTC GCCCCCCAGC GAGAGGAGCT
4981 CTTGCAGCGA GGCGAAGTTT TTCAGCGGCT TGAGTCCGTC GGCCATGGGC ATTTTGGAGA
5041 GGGTCTGTTG CAAGAGTTCC AGACGGTCCC AGAGCTCGGT GATGTGCTCT AGGGCATCTC
5101 GATCCAGCAG ACCTCCTCGT TTCGCGGGTT GGGGCGACTG CGGGAGTAGG GCACCAGGCG
5161 ATGGGCGTCC AGCGAGGCCA GGGTCCGGTC CTTCCAGGGC CGCAGGGTCC GCGTCAGCGT
5221 GGTCTCCGTC ACGGTGAAGG GGTGCGCGCC GGGCTGGGCG CTTGCGAGGG TGCGCTTCAG
5281 GCTCATCCGG CTGGTCGAGA ACCGCTCCCG GTCGGCGCCC TGCGCGTCGG CCAGGTAGCA
5341 ATTGAGCATG AGTTCGTAGT TGAGCGCCTC GGCCGCGTGG CCCTTGGCGC GGAGCTTACC
5401 TTTGGAAGTG TGTCCGCAGA CGGGACAGAG GAGGGACTTG AGGGCGTAGA GCTTGGGGGC
5461 GAGGAAGACG GACTCGGGGG CGTAGGCGTC CGCGCCGCAG CTGGCGCAGA CGGTCTCGCA
5521 CTCCACGAGC CAGGTGAGGT CGGGGCGGTT GGGGTCAAAA ACGAGGTTTC CTCCGTGCTT
5581 TTTGATGCGT TTCTTACCTC TGGTCTCCAT GAGCTCGTGT CCCCGCTGGG TGACAAAGAG
5641 GCTGTCCGTG TCCCCGTAGA CCGACTTTAT GGGCCGGTCC TCGAGCGGGG TGCCGCGGTC
5701 CTCGTCGTAG AGGAACCCCG CCCACTCCGA GACGAAGGCC CGGGTCCAGG CCAGCACGAA
5761 GGAGGCCACG TGGGAGGGGT AGCGGTCGTT GTCCACCAGC GGGTCCACCT TCTCCAGGGT
5821 ATGCAAGCAC ATGTCCCCCT CGTCCACATC CAGGAAGGTG ATTGGCTTGT AAGTGTAGGC
5881 CACGTGACCG GGGGTCCCGG CCGGGGGGGT ATAAAAGGGG GCGGGCCCCT GCTCGTCCTC
5941 ACTGTCTTCC GGATCGCTGT CCAGGAGCGC CAGCTGTTGG GGTAGGTATT CCCTCTCGAA
6001 GGCGGGCATG ACCTCGGCAC TCAGGTTGTC AGTTTCTAGA AACGAGGAGG ATTTGATATT
6061 GACGGTGCCG TTGGAGACGC CTTTCATGAG CCCCTCGTCC ATTTGGTCAG AAAAGACGAT
6121 CTTTTTGTTG TCGAGCTTGG TGGCGAAGGA GCCGTAGAGG GCGTTGGAGA GCAGCTTGGC
6181 GATGGAGCGC ATGGTCTGGT TCTTTTCCTT GTCGGCGCGC TCCTTGGCGG CGATGTTGAG
6241 CTGCACGTAC TCGCGCGCCA CGCACTTCCA TTCGGGGAAG ACGGTGGTGA GCTCGTCGGG
6301 CACGATTCTG ACCCGCCAGC CGCGGTTGTG CAGGGTGATG AGGTCCACGC TGGTGGCCAC
6361 CTCGCCGCGC AGGGGCTCGT TGGTCCAGCA GAGGCGCCCG CCCTTGCGCG AGCAGAAGGG
6421 GGGCAGCGGG TCCAGCATGA GCTCGTCGGG GGGGTCGGCG TCCACGGTGA AGATGCCGGG
6481 CAGGAGCTCG GGGTCGAAGT AGCTGATGCA GGTGCCCAGA TTGTCCAGCG CCGCTTGCCA
6541 GTCGCGCACG GCCAGCGCGC GCTCGTAGGG GCTGAGGGGC GTGCCCCAGG GCATGGGGTG
6601 CGTGAGCGCG GAGGCGTACA TGCCGCAGAT GTCGTAGACG TAGAGGGGCT CCTCGAGGAC
6661 GCCGATGTAG GTGGGGTAGC AGCGCCCCCC GCGGATGCTG GCGCGCACGT AGTCGTACAG
6721 CTCGTGCGAG GGCGCGAGGA GCCCCGTGCC GAGGTTGGAG CGTTGCGGCT TTTCGGCGCG
6781 GTAGACGATC TGGCGGAAGA TGGCGTGGGA GTTGGAGGAG ATGGTGGGCC TTTGGAAGAT
6841 GTTGAAGTGG GCGTGGGGCA GGCCGACCGA GTCCCTGATG AAGTGGGCGT AGGAGTCCTG
6901 CAGCTTGGCG ACGAGCTCGG CGGTGACGAG GACGTCCAGG GCGCAGTAGT CGAGGGTCTC
6961 TTGGATGATG TCATACTTGA GCTGGCCCTT CTGCTTCCAC AGCTCGCGGT TGAGAAGGAA
7021 CTCTTCGCGG TCCTTCCAGT ACTCTTCGAG GGGGAACCCG TCCTGATCGG CACGGTAAGA
7081 GCCCACCATG TAGAACTGGT TGACGGCCTT GTAGGCGCAG CAGCCCTTCT CCACGGGGAG
7141 GGCGTAAGCT TGCGCGGCCT TGCGCAGGGA GGTGTGGGTG AGGGCGAAGG TGTCGCGCAC
7201 CATGACCTTG AGGAACTGGT GCTTGAAGTC GAGGTCGTCG CAGCCGCCCT GCTCCCAGAG
```

Fig. 7B

```
 7261 TTGGAAGTCC GTGCGCTTCT TGTAGGCGGG GTTAGGCAAA GCGAAAGTAA CATCGTTGAA
 7321 GAGGATCTTG CCCGCGCGGG GCATGAAGTT GCGAGTGATG CGGAAAGGCT GGGGCACCTC
 7381 GGCCCGGTTG TTGATGACCT GGGCGGCGAG GACGATCTCG TCGAAGCCGT TGATGTTGTG
 7441 CCCGACGATG TAGAGTTCCA CGAATCGCGG GCGGCCCTTG ACGTGGGGCA GCTTCTTGAG
 7501 CTCGTCGTAG GTGAGCTCGG CGGGGTCGCT GAGCCCGTGC TGCTCGAGGG CCCAGTCGGC
 7561 GACGTGGGGG TTGGCGCTGA GGAAGGAAGT CCAGAGATCC ACGGCCAGGG CGGTCTGCAA
 7621 GCGGTCCCGG TACTGACGGA ACTGTTGGCC CACGGCCATT TTTTCGGGGG TGACGCAGTA
 7681 GAAGGTGCGG GGGTCGCCGT GCCANCGGTC CCACTTGAGC TGGAGGGCGA GGTCGTGGGC
 7741 GAGCTCGACG AGCGGCGGGT CCCCGGAGAG TTTCATGACC AGCATGAAGG GGACGAGCTG
 7801 CTTGCCGAAG GACCCCATCC AGGTGTAGGT TTCCACATCG TAGGTGAGGA AGAGCCTTTC
 7861 GGTGCGAGGA TGCGAGCCGA TGGGGAAGAA CTGGATCTCC TGCCACCAGT TGGAGGAATG
 7921 GCTGTTGATG TGATGGAAGT AGAAATGCCG ACGGCGCGCC GAGCACTCGT GCTTGTGTTT
 7981 ATACAAGCGT CCGCAGTGCT CGCAACGCTG CACGGGATGC ACGTGCTGCA CGAGCTGTAC
 8041 CTGGGTTCCT TTGGCGAGGA ATTTCAGTGG GCAGTGGAGC GCTGGCGGCT GCATCTCGTG
 8101 CTGTACTACG TCTTGGCCAT CGGCGTGGCC ATCGTCTGCC TCGATGGTGG TCATGCTGAC
 8161 GAGCCCGCGC GGGAGGCAGG TCCAGACCTC GGCTCGGACG GGTCGGAGAG CGAGGACGAG
 8221 GGCGCGCAGG CCGGAGCTGT CCAGGGTCCT GAGACGCTGC GGAGTCAGGT CAGTGGGCAG
 8281 CGGCGGCGCG CGGTTGACTT GCAGGAGCTT TTCCAGGGCG CGCGGGAGGT CCAGATGGTA
 8341 CTTGATCTCC ACGGCGCCGT TGGTGGCTAC GTCCACGGCT TGCAGGGTGC CGTGCCCCTG
 8401 GGGCGCCACC ACCGTGCCCC GTTTCTTCTT GGGCGCTGCT TCCATGTCGG TCAGAAGCGG
 8461 CGGCGAGGAC GCGCGCCGGG CGGCAGGGGC GGCTCGGGGC CCGGAGGCAG GGGCGGCAGG
 8521 GGCACGTCGG CGCCGCGCGC GGGCAGGTTC TGGTACTGCG CCCGGAGAAG ACTGGCGTGA
 8581 GCGACGACGC GACGGTTGAC GTCCTGGATC TGACGCCTCT GGGTGAAGGC CACGGGACCC
 8641 GTGAGTTTGA ACCTGAAAGA GAGTTCGACA GAATCAATCT CGGTATCGTT GACGGCGGCC
 8701 TGCCGCAGGA TCTCTTGCAC GTCGCCCGAG TTGTCCTGGT AGGCGATCTC GGTCATGAAC
 8761 TGCTCGATCT CCTCCTCCTG AAGGTCTCCG CGGCCGGCGC GCTCGACGGT GGCCGCGAGG
 8821 TCGTTGGAGA TGCGGCCCAT GAGCTGCGAG AAGGCGTTCA TGCCGGCCTC GTTCCAGACG
 8881 CGGCTGTAGA CCACGGCTCC GTCGGGGTCG CGCGCGCGCA TGACCACCTG GGCGAGGTTG
 8941 AGCTCGACGT GGCGCGTGAA GACCGCGTAG TTGCAGAGGC GCTGGTAGAG GTAGTTGAGC
 9001 GTGGTGGCGA TGTGCTCGGT GACGAAGAAG TACATGATCC AGCGGCGGAG CGGCATCTCG
 9061 CTGACGTCGC CCAGGGCTTC CAAGCGTTCC ATGGCCTCGT AGAAGTCCAC GGCGAAGTTG
 9121 AAAAACTGGG AGTTGCGCGC CGAGACGGTC AACTCCTCCT CCAGAAGACG GATGAGCTCG
 9181 GCGATGGTGG CGCGCACCTC GCGCTCGAAG GCCCCGGGGG GCTCCTCTTC CATCTCCTCC
 9241 TCTTCCTCCT CCACTAACAT CTCTTCTACT TCCTCCTCAG GAGGCGGTGG CGGGGGAGGG
 9301 GCCCTGCGTC GCCGGCGGCG CACGGGCAGA CGGTCGATGA AGCGCTCGAT GGTCTCCCCG
 9361 CGCCGGCGAC GCATGGTCTC GGTGACGGCG CGCCCGTCCT CGCGGGGCCG CAGCATGAAG
 9421 ACGCCGCCGC GCATCTCCAG GTGGCCGCCG GGGGGGTCTC CGTTGGGCAG GGAGAGGGCG
 9481 CTGACGATGC ATCTTATCAA TTGACCCGTA GGGACTCCGC GCAAGGACCT GAGCGTCTCG
 9541 AGATCCACGG GATCCGAAAA CCGCTGAACG AAGGCTTCGA GCCAGTCGCA GTCGCAAGGT
 9601 AGGCTGAGCC CGGTTTCTTG TTCTTCGGGT ATTTGGTCGG GAGGCGGCGG GCGATGCTGC
 9661 TGGTGATGAA GTTGAAGTAG GCGGTCCTGA GACGGCGGAT GGTGGCGAGG AGCACCAGGT
 9721 CCTTGGGCCC GGCTTGCTGG ATGCGCAGAC GGTCGGCCAT GCCCCAGGCG TGGTCCTGAC
 9781 ACCTGGCGAG GTCCTTGTAG TAGTCCTGCA TGAGCCGCTC CACGGGCACC TCCTCCTCGC
 9841 CCGCGCGGCC GTGCATGCGC GTGAGCCCGA ACCCGCGCTG CGGCTGGACG AGCGCCAGGT
 9901 CGGCGACGAC GCGCTCGGTG AGGATGGCCT GCTGGATCTG GGTGAGGGTG GTCTGGAAGT
 9961 CGTCGAAGTC GACGAAGCGG TGGTAGGCTC CGGTGTTGAT GGTGTAGGAG CAGTTGGCCA
10021 TGACGGACCA GTTGACGGTC TGGTGGCCGG GTCGCACGAG CTCGTGGTAC TTGAGGCGCG
10081 AGTAGGCGCG CGTGTCGAAG ATGTAGTCGT TGCAGGCGCG CACGAGGTAC TGGTATCCGA
10141 CGAGGAAGTG CGGCGGCGGC TGGCGGTAGA GCGGCCATCG CTCGGTGGCG GGGGCGCCGG
10201 GCGCGAGGTC CTCGAGCATG AGGCGGTGGT AGCCGTAGAT GTACCTGGAC ATCCAGGTGA
10261 TGCCGGCGGC GGTGGTGGAG GCGCGCGGGA ACTCGCGGAC GCGGTTCCAG ATGTTGCGCA
10321 GCGGCAGGAA GTAGTTCATG GTGGCCGCGG TCTGGCCCGT GAGGCGCGCG CAGTCGTGGA
10381 TGCTCTAGAC ATACGGGCAA AAACGAAAGC GGTCAGCGGC TCGACTCCGT GGCCTGGAGG
10441 CTAAGCGAAC GGGTTGGGCT GCGCGTGTAC CCCGGTTCGA ATCTCGAATC AGGCTGGAGC
10501 CGCAGCTAAC GTGGTACTGG CACTCCCGTC TCGACCCAAG CCTGCTAACG AAACCTCCAG
10561 GATACGGAGG CGGGTCGTTT TTTGGCCTTG GTCGCTGGTC ATGAAAAACT AGTAAGCGCG
10621 GAAAGCGGCC GCCCGCGATG GCTCGCTGCC GTAGTCTGGA GAAAGAATCG CCAGGGTTGC
10681 GTTGCGGTGT GCCCCGGTTC GAGCCTCAGC GCTCGGCGCC GGCCGGATTC CGCGGCTAAC
10741 GTGGGCGTGG CTGCCCCGTC GTTTCCAAGA CCCCTTAGCC AGCCGACTTC TCCAGTTACG
10801 GAGCGAGCCC CTCTTTTTTT TTCTTGTGTT TTTGCCAGAT GCATCCCGTA CTGCGGCAGA
```

Fig. 7C

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10861 TGCGCCCCCA CCCTCCACCA CAACCGCCCC TACCGCAGCA GCAGCAACAG CCGGCGCTTC
10921 TGCCCCCGCC CCAGCAGCAG CCAGCCACTA CCGCGGCGGC CGCCGTGAGC GGAGCCGGCG
10981 TTCAGTATGA CCTGGCCTTG GAAGAGGGCG AGGGGCTGGC GCGGCTGGGG GCGTCGTCGC
11041 CGGAGCGGCA CCCGCGCGTG CAGATGAAAA GGGACGCTCG CGAGGCCTAC GTGCCCAAGC
11101 AGAACCTGTT CAGAGACAGG AGCGGCGAGG AGCCCGAGGA GATGCGCGCC TCCCGCTTCC
11161 ACGCGGGGCG GGAGCTGCGG CGCGGCCTGA ACCGAAAGCG GGTGCTGAGG GACGAGGATT
11221 TCGAGGCGGA CGAGCTGACG GGGATCAGCC CCGTGCGCGC GCACGTGGTC GNGGNCAACC
11281 TGGTCACGGC GTACGAGCAG ACCGTGAAGG AGGAGAGCAA CTTCCAAAAA TCCTTCAACA
11341 ACCACGTGCG CACCTTGATC GCGCGCGAGG AGGTGACCCT GGGCCTGATG CACCTGTGGG
11401 ACCTGCTGGA GGCCATCGTG CAGAACCCCA CGAGCAAGCC GCTGACGGCG CAGCTGTTTC
11461 TGGTGGTGCA GCACAGTCGG GACAACGAGA CGTTCAGGGA GGCGCTGCTG AATATCACCG
11521 AGCCCGAGGG CCGCTGGCTC CTGGACCTGG TGAACATTTT GCAGAGCATC GTGGTGCAGG
11581 AGCGCGGGCT GCCGCTGTCC GAGAAGCTGG CGGCCATCAA CTTCTCGGTG CTGAGTCTGG
11641 GCAAGTACTA CGCTAGGAAG ATCTACAAGA CCCCGTACGT GCCCATAGAC AAGGAGGTGA
11701 AGATCGACGG GTTTTACATG CGCATGACCC TGAAAGTGCT GACCCTGAGC GACGATCTGG
11761 GGGTGTACCG CAACGACAGG ATGCACCGCG CGGTGAGCGC CAGCCGCCGG CGCGAGCTGA
11821 GCGACCAGGA GCTGATGCAC AGCCTGCAGC GGGCCCTGAC CGGGGCCGGG ACCGAGGGGG
11881 AGAGCTACTT TGACATGGGC GCGGACCTGC GCTGGCAGCC CAGCCGCCGG GCCTTGGAAG
11941 CTGCCGGCGG TTCCCCCTAC GTGGAGGAGG TGGACGATGA GGAGGAGGAG GGCGAGTACC
12001 TGGAAGACTG ATGGCGCGAC CGTATTTTTG CTAGATGCAG CAACAGCCAC CGCCGCCGCC
12061 TCCTGATCCC GCGATGCGGG CGGCGCTGCA GAGCCAGCCG TCCGGCATTA ACTCCTCGGA
12121 CGATTGGACC CAGGCCATGC AACGCATCAT GGCGCTGACG ACCCGCAATC CCGAAGCCTT
12181 TAGACAGCAG CCTCAGGCCA ACCGGCTCTC GGCCATCCTG GAGGCCGTGG TGCCCTCGCG
12241 CTCGAACCCC ACGCACGAGA AGGTGCTGGC CATCGTGAAC GCGCTGGTGG AGAACAAGGC
12301 CATCCGCGGT GACGAGGCCG GGCTGGTGTA CAACGCGCTG CTGGAGCGCG TGGCCCGCTA
12361 CAACAGCACC AACGTGCAGA CGAACCTGGA CCGCATGGTG ACCGACGTGC GCGAGGCGGT
12421 GTCGCAGCGC GAGCGGTTCC ACCGCGAGTC GAACCTGGGC TCCATGGTGG CGCTGAACGC
12481 CTTCCTGAGC ACGCAGCCCG CCAACGTGCC CCGGGGCCAG GAGGACTACA CCAACTTCAT
12541 CAGCGCGCTG CGGCTGATGG TGGCCGAGGT GCCCCAGAGC GAGGTGTACC AGTCGGGGCC
12601 GGACTACTTC TTCCAGACCA GTCGCCAGGG CTTGCAGACC GTGAACCTGA GCCAGGCTTT
12661 CAAGAACTTG CAGGGACTGT GGGGCGTGCA GGCCCCGGTC GGGGACCGCG CGACGGTGTC
12721 GAGCCTGCTG ACGCCGAACT CGCGCCTGCT GCTGCTGCTG GTGGCGCCCT TCACGGACAG
12781 CGGCAGCGTG AGCCGCGACT CGTACCTGGG CTACCTGCTT AACCTGTACC GCGAGGCCAT
12841 CGGACAGGCG CACGTGGACG AGCAGACCTA CCAGGAGATC ACCCACGTGA GCCGCGCGCT
12901 GGGCCAGGAG GACCCGGGCA ACCTGGAGGC CACCCTGAAC TTCCTGCTGA CCAACCGGTC
12961 GCAGAAGATC CCGCCCCAGT ACGCGCTGAG CACCGAGGAG GAGCGCATCC TGCGCTACGT
13021 GCAGCAGAGC GTGGGGCTGT TCCTGATGCA GGAGGGGGCC ACGCCCAGCG CGGCGCTCGA
13081 CATGACCGCG CGCAACATGG AGCCCAGCAT GTACGCCCGC AACCGCCCGT TCATCAATAA
13141 GCTGATGGAC TACTTGCATC GGGCGGCCGC CATGAACTCG GACTACTTTA CCAACGCCAT
13201 CTTGAACCCG CACTGGCTCC CGCCGCCCGG GTTCTACACG GGCGAGTACG ACATGCCCGA
13261 CCCCAACGAC GGGTTCCTGT GGGACGACGT GGACAGCAGC GTGTTCTCGC CGCGTCCAGG
13321 AACCAATGCC GTGTGGAAGA AAGAGGGCGG GGACCGGCGG CCGTCCTCGG CGCTGTCCGG
13381 TCGCGCGGGT GCTGCCGCGG CGGTGCCCGA GGCCGCCAGC CCCTTCCCGA GCCTGCCCTT
13441 TTCGCTGAAC AGCGTGCGCA GCAGCGAGCT GGGTCGGCTG ACGCGACCGC GCCTGCTGGG
13501 CGAGGAGGAG TACCTGAACG ACTCCTTGTT GAGGCCCGAG CGCGAGAAGA ACTTCCCCAA
13561 TAACGGGATA GAGAGCCTGG TGGACAAGAT GAGCCGCTGG AAGACGTACG CGCACGAGCA
13621 CAGGGACGAG CCCCGAGCTA GCAGCGCAGG CACCCGTAGA CGCCAGCGGC ACGACAGGCA
13681 GCGGGGACTG GTGTGGGACG ATGAGGATTC CGCCGACGAC AGCAGCGTGT TGGACTTGGG
13741 TGGGAGTGGT GGTAACCCGT TCGCTCACCT GCGCCCCCGT ATCGGGCGCC TGATGTAAGA
13801 ATCTGAAAAA ATAAAAGACG GTACTCACCA AGGCCATGGC GACCAGCGTG CGTTCTTCTC
13861 TGTTGTTTGT AGTAGTATGA TGAGGCGCGT GTACCCGGAG GGTCCTCCTC CCTCGTACGA
13921 GAGCGTGATG CAGCAGGCGG TGGCGGCGGC GATGCAGCCC CCGCTGGAGG CGCCTTACGT
13981 GCCCCCGCGG TACCTGGCGC CTACGGAGGG GCGGAACAGC ATTCGTTACT CGGAGCTGGC
14041 ACCCTTGTAC GATACCACCC GGTTGTACCT GGTGGACAAC AAGTCGGCAG ACATCGCCTC
14101 GCTGAACTAC CAGAACGACC ACAGCAACTT CCTGACCACC GTGGTGCAGA ACAACGATTT
14161 CACCCCCACG GAGGCCAGCA CCCAGACCAT CAACTTTGAC GAGCGCTCGC GGTGGGGCGG
14221 CCAGCTGAAA ACCATCATGC ACACCAACAT GCCCAACGTG AACGAGTTCA TGTACAGCAA
14281 CAAGTTCAAG GCGCGGGTGA TGGTCTCGCG CAAGACCCCC AACGGGGTGG ATGATGATTA
14341 TGATGGTAGT CAGGACGAGC TGACCTACGA GTGGGTGGAG TTTGAGCTGC CCGAGGGCAA
14401 CTTCTCGGTG ACCATGACCA TCGATCTGAT GAACAACGCC ATCATCGACA ACTACTTGGC
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Fig. 7D

SEQ ID NO: 3


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14461 GGTGGGGCGG CAGAACGGGG TGCTGGAGAG CGACATCGGC GTGAAGTTCG ACACGCGCAA
14521 CTTCCGGCTG GGCTGGGACC CCGTGACCGA GCTGGTGATG CCGGGCGTGT ACACCAACGA
14581 GGCCTTCCAC CCCGACATCG TCCTGCTGCC CGGCTGCGGC GTGGACTTCA CCGAGAGCCG
14641 CCTCAGCAAC CTGCTGGGCA TCCGCAAGCG GCAGCCCTTC CAGGAGGGCT TCCAGATCCT
14701 GTACGAGGAC CTGGAGGGGG GCAACATCCC CGCGCTCTTG GATGTCGAAG CCTACGAGAA
14761 AAGCAAGGAG GATAGCACCG CCGCGGCGAC CGCAGCCGTG GCCACCGCCT CTACCGAGGT
14821 GCGGGGCGAT AATTTTGCTA GCGCTGCGGC AGCGGCCGAG GCGGCTGAAA CCGAAAGTAA
14881 GATAGTCATC CAGCCGGTGG AGAAGGACAG CAAGGACAGG AGCTACAACG TGCTCGCGGA
14941 CAAGAAAAAC ACCGCCTACC GCAGCTGGTA CCTGGCCTAC AACTACGGCG ACCCCGAGAA
15001 GGGCGTGCGC TCCTGGACGC TGCTCACCAC CTCGGACGTC ACCTGCGGCG TGGAGCAAGT
15061 CTACTGGTCG CTGCCCGACA TGATGCAAGA CCCGGTCACC TTCCGCTCCA CGCGTCAAGT
15121 TAGCAACTAC CCGGTGGTGG GCGCCGAGCT CCTGCCCGTC TACTCCAAGA GCTTCTTCAA
15181 CGAGCAGGCC GTCTACTCGC AGNAGCTGCG CGCCTTCACC TCGCTCACGC ACGTCTTCAA
15241 CCGCTTCCCC GAGAACCAGA TCCTCGTCCG CCGCCGCGCC CACCATTACC ACCGTCAGTG
15301 AAAACGTTCC TGCTCTCACA GATCACGGGA CCCTGCCGCT GCGCAGCAGT ATCCGGGGAG
15361 TCCAGCGCGT GACCGTCACT GACGCCAGAC GCCGCACCTG CCCCTACGTC TACAAGGCCC
15421 TGGGCGTAGT CGCGCCGCGC GTCCTCTCGA GCCGCACCTT CTAAAAAATG TCCATTCTCA
15481 TCTCGCCCAG TAATAACACC GGTTGGGGCC TGCGCGCGCC CAGCAAGATG TACGGAGGCG
15541 CTCGCCAACG CTCCACGCAA CACCCCGTGC GCGTGCGCGG GCACTTCCGC GCTCCCTGGG
15601 GCGCCCTCAA GGGCCGCGTG CGCTCGCGCA CCACCGTCGA CGACGTGATC GACCAGGTGG
15661 TGGCCGACGC GCGCAACTAC ACGCCCGCCG CCGCGCCCGT CTCCACCGTG GACGCCGTCA
15721 TCGACAGCGT GGTGGCCGAC GCGCGCCGGT ACGCCCGCAC CAAGAGCCGG CGGCGGCGCA
15781 TCGCCCGGCG GCACCGGAGC ACCCCCGCCA TGCGCGCGGC GCGAGCCTTG CTGCGCAGGG
15841 CCAGGCGCAC GGGACGCAGG GCCATGCTCA GGGCGGCCAG ACGCGCGGCC TCCGGCAGCA
15901 GCAGCGCCGG CAGGACCCGC AGACGCGCGG CCACGGCGGC GGCGGCGGCC ATCGCCAGCA
15961 TGTCCCGCCC GCGGCGCGGC AACGTGTACT GGGTGCGCGA CGCCGCCACC GGTGTGCGCG
16021 TGCCCGTGCG CACCCGCCCC CCTCGCACTT GAAGATGCTG ACTTCGCGAT GTTGATGTGT
16081 CCCAGCGGCG AGGAGGATGT CCAAGCGCAA ATACAAGGAA GAGATGCTCC AGGTCATCGC
16141 GCCTGAGATC TACGGCCCCG CGGCGGCGGT GAAGGAGGAA AGAAAGCCCC GCAAACTGAA
16201 GCGGGTCAAA AAGGACAAAA AGGAGGAGGA AGATGACGGA CTGGTGGAGT TTGTGCGCGA
16261 GTTCGCCCCC CGGCGGCGCG TGCAGTGGCG CGGGCGGAAA GTGAAACCGG TGCTGCGGCC
16321 CGGCACCACG GTGGTCTTCA CGCCCGGCGA GCGTTCCGGC TCCGCCTCCA AGCGCTCCTA
16381 CGACGAGGTG TACGGGGACG AGGACATCCT CGAGCAGGCG GTCGAGCGTC TGGGCGAGTT
16441 TGCGTACGGC AAGCGCAGCC GCCCCGCGCC CTTGAAAGAG GAGGCGGTGT CCATCCCGCT
16501 GGACCACGGC AACCCCACGC CGAGCCTGAA GCCGGTGACC CTGCAGCAGG TGCTACCGAG
16561 CGCGGCGCCG CGCCGGGGCT TCAAGCGCGA GGGCGGCGAG GATCTGTACC CGACCATGCA
16621 GCTGATGGTG CCCAAGCGCC AGAAGCTGGA GGACGTGCTG GAGCACATGA AGGTGGACCC
16681 CGAGGTGCAG CCCGAGGTCA AGGTGCGGCC CATCAAGCAG GTGGCCCCGG GCCTGGGCGT
16741 GCAGACCGTG GACATCAAGA TCCCCACGGA GCCCATGGAA ACGCAGACCG AGCCCGTGAA
16801 GCCCAGCACC AGCACCATGG AGGTGCAGAC GGATCCCTGG ATGCCAGCAC CAGCTTCCAC
16861 CAGCACTCGC CGAAGACGCA AGTACGGCGC GGCCAGCCTG CTGATGCCCA ACTACGCGGC
16921 TGCATCCTTC CATCATCCCC ACGCCGGGCT ACCGCGGCAC GCGCTTCTAC CGCGGCTACA
16981 CCAGCAGCCG CCGCCGCAAG ACCACCACCC GCCGCCGTCG TCGCAGCCGC CGCAGCAGCA
17041 CCGCGACTTC CGCCTTGGTG CGGAGAGTGT ATCGCAGCGG GCGCGAGCCT CTGACCCTGC
17101 CGCGCGCGCG CTACCACCCG AGCATCGCCA TTTAACTACC GCCTCCTACT TGCAGATATG
17161 GCCCTCACAT GCCGCCTCCG CGTCCCCATT ACGGGCTACC GAGGAAGAAA GCCGCGCCGT
17221 AGAAGGCTGA CGGGGAACGG GCTGCGTCGC CATCACCACC GGCGGCGGCG CGCCATCAGC
17281 AAGCGGTTGG GGGGAGGCTT CCTGCCCGCG CTGATCCCCA TCATCGCCGC GGCGATCGGG
17341 GCGATCCCCG GCATAGCTTC CGTGGCGGTG CAGGCCTCTC AGCGCCACTG AGACACAAAA
17401 AAGCATGGAT TTGTAATAAA AAAAAAAATG GACTGACGCT CCTGGTCCTG TGATGTGTGT
17461 TTTTAGATGG AAGACATCAA TTTTTCGTCC CTGGCACCGC GACACGGCAC GCGGCCGTTT
17521 ATGGGCACCT GGAGCGACAT CGGCAACAGC CAACTGAACG GGGGCGCCTT CAATTGGAGC
17581 AGTCTCTGGA GCGGGCTTAA GAATTTCGGG TCCACGCTCA AAACCTATGG CAACAAGGCG
17641 TGGAACAGCA GCACAGGGCA GGCGCTGAGG GAAAAGCTGA AAGAACAGAA CTTCCAGCAG
17701 AAGGTGGTTG ATGGCCTGGC CTCAGGCATC AACGGGGTGG TTGACCTGGC CAACCAGGCC
17761 GTGCAGAAAC AGATCAACAG CCGCCTGGAC GCGGTCCCGC CCGCGGGGTC CGTGGAGATG
17821 CCCCAGGTGG AGGAGGAGCT GCCTCCCCTG GACAAGCGCG GCGACAAGCG ACCGCGTCCC
17881 GACGCGGAGG AGACGCTGCT GACGCACACG GACGAGCCGC CCCCGTACGA GGAGGCGGTG
17941 AAACTGGGCC TGCCCACCAC GCGGCCCGTG GCGCCTCTGG CCACCGGAGT GCTGAAACCC
18001 AGCAGCAGCC AGCCCGCGAC CCTGGACTTG CCTCCGCCTC GCCCCTCCAC AGTGGCTAAG
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Fig. 7E

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18061 CCCCTGCCGC CGGTGGCCGT CGCGTCGCGC GCCCCCCGAG GCCGCCCCCA GGCGAACTGG
18121 CAGAGCACTC TGAACAGCAT CGTGGGTCTG GGAGTGCAGA GTGTGAAGCG CCGCCGCTGC
18181 TATTAAAAGA CACTGTAGCG CTTAACTTGC TTGTCTGTGT GTATATGTAT GTCCGCCGAC
18241 CAGAAGGAGG AGTGTGAAGA GGCGCGTCGC CGAGTTGCAA GATGGCCACC CCATCGATGC
18301 TGCCCCAGTG GGCGTACATG CACATCGCCG GACAGGACGC TTCGGAGTAC CTGAGTCCGG
18361 GTCTGGTGCA GTTCGCCCGC GCCACAGACA CCTACTTCAG TCTGGGGAAC AAGTTTAGGA
18421 ACCCCACGGT GGCGCCCACG CACAATGTGA CCACCGACCG CAGCCAGCGG CTGACGGTGC
18481 GCTTCGTGCC CGTGGACCGC GAGGACAACA CCTACTCGTA CAAAGTGCGC TACACGCTGG
18541 CCGTGGGCGA CAACCGCGTG CTGGACATGG CCAGCACCTA CTTTGACATC CGCGGCGTGC
18601 TGGACCGGGG CCCTAGCTTC AAACCCTACT CTGGCACCGC CTACAACAGC CTAGCTCCCA
18661 AGGGAGCTCC CAATTCCAGC CAGTGGGAGC AAGCAAAAAC AGGCAATGGG GGAACTATGG
18721 AAACACACAC ATATGGTGTG GCCCCAATGG GCGGAGAGAA TATTACAAAA GATGGTCTTC
18781 AAATTGGAAC TGACGTTACA GCGAATCAGA ATAAACCAAT TTATGCCGAC AAAACATTTC
18841 AACCAGAACC GCAAGTAGGA GAAGAAAATT GGCAAGAAAC TGAAAACTTT TATGGCGGTA
18901 GAGCTCTTAA AAAAGACACA AACATGAAAC CTTGCTATGG CTCCTATGCT AGACCCACCA
18961 ATGAAAAAGG AGGTCAAGCT AAACTTAAAG TTGGAGATGA TGGAGTTCCA ACCAAAGAAT
19021 TCGACATAGA CCTGGCTTTC TTTGATACTC CCGGTGGCAC CGTGAACGGT CAAGACGAGT
19081 ATAAAGCAGA CATTGTCATG TATACCGAAA ACACGTATTT GGAAACTCCA GACACGCATG
19141 TGGTATACAA ACCAGGCAAG GATGATGCAA GTTCTGAAAT TAACCTGGTT CAGCAGTCTA
19201 TGCCCAACAG ACCCAACTAC ATTGGGTTCA GGGACAACTT TATCGGTCTT ATGTACTACA
19261 ACAGCACTGG CAATATGGGT GTGCTTGCTG GTCAGGCCTC CCAGCTGAAT GCTGTGGTTG
19321 ATTTGCAAGA CAGAAACACC GAGCTGTCCT ACCAGCTCTT GCTTGACTCT TTGGGTGACA
19381 GAACCCGGTA TTTCAGTATG TGGAACCAGG CGGTGGACAG TTATGACCCC GATGTGCGCA
19441 TCATCGAAAA CCATGGTGTG GAGGATGAAT TGCCAAACTA TTGCTTCCCC TTGGACGGCT
19501 CTGGCACTAA CGCCGCATAC CAAGGTGTGA AAGTAAAAGA TGGTCAAGAT GGTGATGTTG
19561 AGAGTGAATG GGAAAATGAC GATACTGTTG CAGCTCGAAA TCAATTATGT AAAGGTAACA
19621 TTTTCGCCAT GGAGATTAAT CTCCAGGCTA ACCTGTGGAG AAGTTTCCTC TACTCGAACG
19681 TGGCCCTGTA CCTGCCCGAC TCCTACAAGT ACACGCCGAC CAACGTCACG CTGCCGACCA
19741 ACACCAACAC CTACGATTAC ATGAATGGCA GAGTGACACC TCCCTCGCTG GTAGACGCCT
19801 ACCTCAACAT CGGGGCGCGC TGGTCGCTGG ACCCCATGGA CAACGTCAAC CCCTTCAACC
19861 ACCACCGCAA CGCGGGCCTG CGCTACCGCT CCATGCTCCT GGGCAACGGG CGCTACGTGC
19921 CCTTCCACAT CCAGGTGCCC CAAAAGTTTT TCGCCATCAA GAGCCTCCTG CTCCTGCCCG
19981 GGTCCTACAC CTACGAGTGG AACTTCCGCA AGGACGTCAA CATGATCCTG CAGAGCTCCC
20041 TAGGCAACGA CCTGCGCACG GACGGGGCCT CCATCGCCTT CACCAGCATC AACCTCTACG
20101 CCACCTTCTT CCCCATGGCG CACAACACCG CCTCCACGCT CGAGGCCATG CTGCGCAACG
20161 ACACCAACGA CCAGTCCTTC AACGACTACC TCTCGGCGGC CAACATGCTC TACCCCATCC
20221 CGGCCAACGC CACCAACGTG CCCATCTCCA TCCCCTCGCG CAACTGGGCC GCCTTCCGCG
20281 GATGGTCCTT CACGCGCCTG AAGACCCGCG AGACGCCCTC GCTCGGCTCC GGGTTCGACC
20341 CCTACTTCGT CTACTCGGGC TCCATCCCCT ACCTAGACGG CACCTTCTAC CTCAACCACA
20401 CCTTCAAGAA GGTCTCCATC ACCTTCGACT CCTCCGTCAG CTGGCCCGGC AACGACCGCC
20461 TCCTGACGCC CAACGAGTTC GAAATCAAGC GCACCGTCGA CGGAGAGGGA TACAACGTGG
20521 CCCAGTGCAA CATGACCAAG GACTGGTTCC TGGTCCAGAT GCTGGCCCAC TACAACATCG
20581 GCTACCAGGG CTTCTACGTG CCCGAGGGCT ACAAGGACCG CATGTACTCC TTCTTCCGCA
20641 ACTTCCAGCC CATGAGCCGC CAGGTCGTGG ACGAGGTCAA CTACAAGGAC TACCAGGCCG
20701 TCACCCTGGC CTACCAGCAC AACAACTCGG GCTTCGTCGG CTACCTCGCG CCCACCATGC
20761 GCCAGGGCCA GCCCTACCCC GCCAACTACC CCTACCCGCT CATCGGCAAG AGCGCCGTCG
20821 CCAGCGTCAC CCAGAAAAAG TTCCTCTGCG ACCGGGTCAT GTGGCGCATC CCCTTCTCCA
20881 GCAACTTCAT GTCCATGGGC GCGCTCACCG ACCTCGGCCA GAACATGCTC TACGCCAACT
20941 CCGCCCACGC GCTAGACATG AATTTCGAAG TCGACCCCAT GGATGAGTCC ACCCTTCTCT
21001 ATGTTGTCTT CGAAGTCTTC GACGTCGTCC GAGTGCACCA GCCCCACCGC GGCGTCATCG
21061 AAGCCGTCTA CCTGCGCACG CCCTTCTCGG CCGGCAACGC CACCACCTAA GCCGCTCTTG
21121 CTTCTTGCAA GATGACGGCG GGCTCCGGCG AGCAGGAGCT CAGGGCCATC CTCCGCGACC
21181 TGGGCTGCGG GCCCTGCTTC CTGGGCACCT TCGACAAGCG CTTCCCTGGA TTCATGGCCC
21241 CGCACAAGCT GGCCTGCGCC ATCGTGAACA CGGCCGGCCG CGAGACCGGG GGCGAGCACT
21301 GGCTGGCCTT CGCCTGGAAC CCGCGCTCCC ACACATGCTA CCTCTTCGAC CCCTTCGGGT
21361 TCTCGGACGA GCGCCTCAAG CAGATCTACC AGTTCGAGTA CGAGGGCCTG CTGCGTCGCA
21421 GCGCCCTGGC CACCGAGGAC CGCTGCGTCA CCCTGGAAAA GTCCACCCAG ACCGTGCAGG
21481 GTCCGCGCTC GGCCGCCTGC GGGCTCTTCT GCTGCATGTT CCTGCACGCC TTCGTGCACT
21541 GGCCCGACCG CCCCATGGAC AAGAACCCCA CCATGAACTT ACTGACGGGG GTGCCCAACG
21601 GCATGCTCCA GTCGCCCCAG GTGGAACCCA CCCTGCGCCG CAACCAGGAA GCGCTCTACC
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Fig. 7F

SEQ ID NO: 3


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21661 GCTTCCTCAA TGCCCACTCC GCCTACTTTC GCTCCCACCG CGCGCGCATC GAGAAGGCCA
21721 CCGCCTTCGA CCGCATGAAT CAAGACATGT AAAAAACCGG TGTGTGTATG TGAATGCTTT
21781 ATTCATAATA AACAGCACAT GTTTATGCCA CCTTCTCTGA GGCTCTGACT TTATTTAGAA
21841 ATCGAAGGGG TTCTGCCGGC TCTCGGCATG GCCCGCGGGC AGGGATACGT TGCGGAACTG
21901 GTACTTGGGC AGCCACTTGA ACTCGGGGAT CAGCAGCTTG GGCACGGGGA GGTCGGGGAA
21961 CGAGTCGCTC CACAGCTTGC GCGTGAGTTG CAGGGCGCCC AGCAGGTCGG GCGCGGAGAT
22021 CTTGAAATCG CAGTTGGGAC CCGCGTTCTG CGCGCGAGAG TTGCGGTACA CGGGGTTGCA
22081 GCACTGGAAC ACCATCAGGG CCGGGTGCTT CACGCTTGCC AGCACCGTCG CGTCGGTGAT
22141 GCCCTCCACG TCCAGATCCT CGGCGTTGGC CATCCCGAAG GGGGTCATCT TGCAGGTCTG
22201 CCGCCCCATG CTGGGCACGC AGCCGGGCTT GTGGTTGCAA TCGCAGTGCA GGGGGATCAG
22261 CATCATCTGG GCCTGCTCGG AGCTCATGCC CGGGTACATG GCCTTCATGA AAGCCTTCAG
22321 CTGGCGGAAG GCCTGCTGCG CCTTGCCGCC CTCGGTGAAG AAGACCCCGC AGGACTTGCT
22381 AGAGAACTGG TTGGTGGCGC AGCCGGCGTC GTGCACGCAG CAGCGCGCGT CGTTGTTGGC
22441 CAGCTGCACC ACGCTGCGCC CCCAGCGGTT CTGGGTGATC TTGGCCCGGT TGGGGTTCTC
22501 CTTCAGCGCG CGCTGCCCGT TCTCGCTCGC CACATCCATC TCGATAGTGT GCTCCTTCTG
22561 GATCATCACG GTCCCGTGCA GGCACCGCAG CTTGCCCTCG GCTTCGGTGC AGCCGTGCAG
22621 CCACAGCGCG CAGCCGGTGC ACTCCCAGTT CTTGTGGGCG ATCTGGGAGT GCGAGTGCAC
22681 GAAGCCCTGC AGGAAGCGGC CCATCATCGC GGTCAGGGTC TTGTTGCTGG TGAAGGTCAG
22741 CGGGATGCCG CGGTGCTCCT CGTTCACATA CAGGTGGCAG ATGCGGCGGT ACACCTCGCC
22801 CTGCTCGGGC ATCAGCTGGA AGGCGGACTT CAGGTCGCTC TCCACGCGGT ACCGGTCCAT
22861 CAGCAGCGTC ATCACTTCCA TGCCCTTCTC CCAGGCCGAA ACGATCGGCA GGCTCAGGGG
22921 GTTCTTCACC GCCATTGTCA TCTTAGTCGC CGCCGCCGAG GTCAGGGGGT CGTTCTCGTC
22981 CAGGGTCTCA AACACTCGCT TGCCGTCCTT CTCGATGATG CGCACGGGGG GAAAGCTGAA
23041 GCCCACGGCC GCCAGCTCCT CCTCGGCCTG CCTTTCGTCC TCGCTGTCCT GGCTGATGTC
23101 TTGCAAAGGC ACATGCTTGG TCTTGCGGGG TTTCTTTTTG GGCGGCAGAG GCGGCGGCGA
23161 TGTGCTGGGA GAGCGCGAGT TCTCGTTCAC CACGACTATT TCTTCTTCTT GGCCGTCGTC
23221 CGAGACCACG CGGCGGTAGG CATGCCTCTT CTGGGGCAGA GGCGGAGGCG ACGGGCTCTC
23281 GCGGTTCGGC GGGCGGCTGG CAGAGCCCCT TCCGCGTTCG GGGGTGCGCT CCTGGCGGCG
23341 CTGCTCTGAC TGACTTCCTC CGCGGCCGGC CATTGTGTTC TCCTAGGGAG CAACAACAAG
23401 CATGGAGACT CAGCCATCGT CGCCAACATC GCCATCTGCC CCCGCCGCCA CCGCCGACGA
23461 GAACCAGCAG CAGAATGAAA GCTTAACCGC CCCGCCGCCC AGCCCCACCT CCGACGCCGC
23521 GGCCCCAGAC ATGCAAGAGA TGGAGGAATC CATCGAGATT GACCTGGGCT ACGTGACGCC
23581 CGCGGAGCAC GAGGAGGAGC TGGCAGCGCG CTTTTCAGCC CCGGAAGAGA ACCACCAAGA
23641 GCAGCCAGAG CAGGAAGCAG AGAACGAGCA GAACCAGGCT GGGCACGAGC ATGGCGACTA
23701 CCTGAGCGGG GCAGAGGACG TGCTCATCAA GCATCTGGCC CGCCAATGCA TCATCGTCAA
23761 GGACGCGCTG CTCGACCGCG CCGAGGTGCC CCTCAGCGTG GCGGAGCTCA GCCGCGCCTA
23821 CGAGCGCAAC CTCTTCTCGC CGCGCGTGCC CCCCAAGCGC CAGCCCAACG GCACCTGTGA
23881 GCCCAACCCG CGCCTCAACT TCTACCCGGT CTTCGCGGTG CCCGAGGCCC TGGCCACCTA
23941 CCACCTCTTT TTCAAGAACC AAAGGATCCC CGTCTCCTGC CGCGCCAACC GCACCCGCGC
24001 CGACGCCCTG CTCAACCTGG GCCCCGGCGC CCGCCTACCT GATATCACCT CCTTGGAAGA
24061 GGTTCCCAAG ATCTTCGAGG GTCTGGGCAG CGACGAGACT CGGGCCGCGA ACGCTCTGCA
24121 AGGAAGCGGA GAGGAGCATG AGCACCACAG CGCCCTGGTG GAGTTGGAAG GCGACAACGC
24181 GCGCCTGGCG GTCCTCAAGC GCACGGTCGA GCTGACCCAC TTCGCCTACC CGGCGCTCAA
24241 CCTGCCCCCC AAGGTCATGA GCGCCGTCAT GGACCAGGTG CTCATCAAGC GCGCCTCGCC
24301 CCTCTCGGAG GAGGAGATGC AGGACCCCGA GAGTTCGGAC GAGGGCAAGC CCGTGGTCAG
24361 CGACGAGCAG CTGGCGCGCT GGCTGGGAGC GAGTANCACC CCCCAGAGCC TGGAAGAGCG
24421 GCGCAAGCTC ATGATGGCCG TGGTCCTGGT GACCGTGGAG CTGGAGTGTC TGCGCCGCTT
24481 CTTTGCCGAC GCGGAGACCC TGCGCAAGGT CGAGGAGAAC CTGCACTACC TCTTCAGGCA
24541 CGGGTTCGTG CGCCAGGCCT GCAAGATCTC CAACGTGGAG CTGACCAACC TGGTCTCCTA
24601 CATGGGCATC CTGCACGAGA ACCGCCTGGG GCAAAACGTG CTGCACACCA CCCTGCGCGG
24661 GGAGGCCCGC CGCGACTACA TCCGCGACTG CGTCTACCTG TACCTCTGCC ACACCTGGCA
24721 GACGGGCATG GGCGTGTGGC AGCAGTGCCT GGAGGAGCAG AACCTGAAAG AGCTCTGCAA
24781 GCTCCTGCAG AAGAACCTCA AGGCCCTGTG GACCGGGTTC GACGAGCGTA CCACCGCCTC
24841 GGACCTGGCC GACCTCATCT TCCCCGAGCG CCTGCGGCTG ACGCTGCGCA ACGGGCTGCC
24901 CGACTTTATG AGCCAAAGCA TGTTGCAAAA CTTTCGCTCT TTCATCCTCG AACGCTCCGG
24961 GATCCTGCCC GCCACCTGCT CCGCGCTGCC CTCGGACTTC GTGCCGCTGA CCTTCCGCGA
25021 GTGCCCCCCG CCGCTCTGGA GCCACTGCTA CTTGCTGCGC CTGGCCAACT ACCTGGCCTA
25081 CCACTCGGAC GTGATCGAGG ACGTCAGCGG CGAGGGTCTG CTGGAGTGCC ACTGCCGCTG
25141 CAACCTCTGC ACGCCGCACC GCTCCCTGGC CTGCAACCCC CAGCTGCTGA GCGAGACCCA
25201 GATCATCGGC ACCTTCGAGT TGCAAGGCCC CGGCGACGGC GAGGGCAAGG GGGGTCTGAA
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Fig. 7G

SEQ ID NO: 3


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25261 ACTCACCCCG GGGCTGTGGA CCTCGGCCTA CTTGCGCAAG TTCGTGCCCG AGGACTACCA
25321 TCCCTTCGAG ATCAGGTTCT ACGAGGACCA ATCCCAGCCG CCCAAGGCCG AGCTGTCGGC
25381 CTGCGTCATC ACCCAGGGGG CCATCCTGGC CCAATTGCAA GCCATCCAGA AATCCCGCCA
25441 AGAATTTCTG CTGAAAAAGG GCCACGGGGT CTACTTGGAC CCCCAGACCG GAGAGGAGCT
25501 CAACCCCAGC TTCCCCCAGG ATGCCCCGAG GAAGCAGCAA GAAGCTGAAA GTGGAGCTGC
25561 CGCCGCCGGA GGATTTGGAG GAAGACTGGG AGAGCAGTCA GGCAGAGGAG GAGGAGATGG
25621 AAGACTGGGA CAGCACTCAG GCAGAGGAGG ACAGCCTGCA AGACAGTCTG GAGGAGGAAG
25681 ACGAGGTGGA GGAGGCAGAG GAAGAAGCAG CCGCCGCCAG ACCGTCGTCC TCGGCGGAGA
25741 AAGCAAGCAG CACGGATACC ATCTCCGCTC CGGGTCGGGG TCGCGGCGGC CGGGCCCACA
25801 GTAGGTGGGA CGAGACCGGG CGCTTCCGAA CCCCACCACC CAGACCGGTA AGAAGGAGCG
25861 GCAGGGATAC AAGTCCTGGC GGGGGCACAA AAACGCCATC GTCTCCTGCT TGCAAGCCTG
25921 CGGGGGCAAC ATCTCCTTCA CCCGGCGCTA CCTGCTCTTT CACCGCGGGG TGAACTTCCC
25981 CCGCAACATC TTGCATTACT ACCGTCACCT CCACAGCCCC TACTACTGTT TCCAAGAAGA
26041 GGCAGAAACC CAGCAGCAGC AGAAAACCAG CGGCAGCAGC AGCTAGAAAA TCCACAGCGG
26101 CGGCAGGTGG ACTGAGGATC GCGGCGAACG AGCCGGCGCA GACCCGGGAG CTGAGGAACC
26161 GGATCTTTCC CACCCTCTAT GCCATCTTCC AGCAGAGTCG GGGGCAGGAG CAGGAACTGA
26221 AAGTCAAGAA CCGTTCTCTG CGCTCGCTCA CCCGCAGTTG TCTGTATCAC AAGAGCGAAG
26281 ACCAACTTCA GCGCACTCTC GAGGACGCCG AGGCTCTCTT CAACAAGTAC TGCGCGCTCA
26341 CTCTTAAAGA GTAGCCCGCG CCCGCCCACA CACGGAAAAA GGCGGGAATT ACGTCACCAC
26401 CTGCGCCCTT CGCCCGACCA TCATGAGCAA AGAGATTCCC ACGCCTTACA TGTGGAGCTA
26461 CCAGCCCCAG ATGGGCCTGG CCGCCGGCGC CGCCCAGGAC TACTCCACCC GCATGAACTG
26521 GCTCAGTGCC GGGCCCGCGA TGATCTCACG GGTGAATGAC ATCCGCGCCC ACCGAAACCA
26581 GATACTCCTA GAACAGTCAG CGATCACCGC CACGCCCCGC CATCACCTTA ATCCGCGTAA
26641 TTGGCCCGCC GCCCTGGTGT ACCAGGAAAT TCCCCAGCCC ACGACCGTAC TACTTCCGCG
26701 AGACGCCCAG GCCGAAGTCC AGCTGACTAA CTCAGGTGTC CAGCTGGCCG GCGGCGCCGC
26761 CCTGTGTCGT CACCGCCCCG CTCAGGGTAT AAAGCGGCTG GTGATCCGAG GCAGAGGCAC
26821 ACAGCTCAAC GACGAGGTGG TGAGCTCTTC GCTGGGTCTG CGACCTGACG GAGTCTTCCA
26881 ACTCGCCGGA TCGGGGAGAT CTTCCTTCAC GCCTCGTCAG GCCGTCCTGA CTTTGGAGAG
26941 TTCGTCCTCG CAGCCCCGCT CGGGCGGCAT CGGCACTCTC CAGTTCGTGG AGGAGTTCAC
27001 TCCCTCGGTN TACTTCAACC CCTTCTCCGG CTCCCCCGGC CACTACCCGG ACGAGTTCAT
27061 CCCGAACTTC GACGCCATCA GCGAGTCGGT GGACGGCTAC GATTGAATGT CCCATGGTGG
27121 CGCAGCTGAC CTAGCTCGGC TTCGACACCT GGACCACTGC CGCCGCTTCC GCTGCTTCGC
27181 TCGGGATCTC GCCGAGTTTG CCTACTTTGA GCTGCCCGAG GAGCACCCTC AGGGCCCAGC
27241 CCACGGAGTG CGGATCATCG TCGAAGGGGG CCTCGACTCC CACCTGCTTC GGATCTTCAG
27301 CCAGCGACCG ATCCTGGTCG AGCGCGAACA AGGACAGACC CTTCTTACTT TGTACTGCAT
27361 CTGCAACCAC CCCGGCCTGC ATGAAAGTCT TTGTTGTCTG CTGTGTACTG AGTATAATAA
27421 AAGCTGAGAT CAGCGACTAC TCCGGACTCG ATTGTGGTGT TCCTGCTATC AACCGGTCCC
27481 TGTTCTTCAC CGGGAACGAG ACCGAGCTCC AGCTCCAGTG TAAGCCCCAC AAGAAGTACC
27541 TCACCTGGCT GTTCCAGGGC TCCCCGATCG CCGTTGTCAA CCACTGCGAC AACGACGGAG
27601 TCCTGCTGAG CGGCCCTGCC AACCTTACTT TTTCCACCCG CAGAAGCAAG CTCCAGCTCT
27661 TCCAACCCTT CCTCCCCGGG ACCTATCAGT GCGTCTCAGG ACCCTGCCAT CACACCTTCC
27721 ACCTGATCCC GAATACCACA GCGCCGCTCC CCGCTACTAA CAACCAAACT ACCCACCAAC
27781 GCCACCGTCG CGACCTTTCC TCTGAATCTA ATACCACTAC CGGAGGTGAG CTCCGAGGTC
27841 GACCAACCTC TGGGATTTAC TACGGCCCCT GGGAGGTGGT GGGGTTAATA GCGCTAGGCC
27901 TAGTTGCGGG TGGGCTTTTG GTTCTCTGCT ACCTATACCT CCCTTGCTGT TCGTACTTAG
27961 TGGTGCTGTG TTGCTGGTTT AAGAAATGGG GAAGATCACC CTAGTGAGCT GCGGTGCGCT
28021 GGTGGCGGTG TTGCTTTCGA TTGTGGGACT GGGCGGCGCG GCTGTAGTGA AGGAGAAGGC
28081 CGATCCCTGC TTGCATTTCA ATCCCAACAA ATGCCAGCTG AGTTTTCAGC CCGATGGCAA
28141 TCGGTGCGCG GTACTGATCA AGTGCGGATG GGAATGCGAG AACGTGAGAA TCGAGTACAA
28201 TAACAAGACT CGGAACAATA CTCTCGCGTC CGTGTGGCAG CCCGGGGACC CCGAGTGGTA
28261 CACCGTCTCT GTCCCCGGTG CTGACGGCTC CCCGCGCACC GTGAATAATA CTTTCATTTT
28321 TGCGCACATG TGCAACACGG TCATGTGGAT GAGCAAGCAG TACGATATGT GGCCCCCCAC
28381 GAAGGAGAAC ATCGTGGTCT TCTCCATCGC TTACAGCCTG TGCACGGCGC TAATCACCGC
28441 TATCGTGTGC CTGAGCATTC ACATGCTCAT CGCTATTCGC CCCAGAAATA ATGCCGAGAA
28501 AGAGAAACAG CCATAACACG TTTTTTCACA CACCTTGTTT TTACAGACAA TGCGTCTGTT
28561 AAATTTTTTA AACATTGTGC TCAGTATTGC TTATGCCTCT GGTTATGCAA ACATACAGAA
28621 AACCCTTTAT GTAGGATCTG ATGGTACACT AGAGNGTACC CAATCACAAG CCAAGGTTGC
28681 ATGGTATTTT TATAGAACCA ACACTGATCC AGTTAAACTT TGTAAGGGTG AATTGCCGCG
28741 TACACATAAA ACTCCACTTA CATTTAGTTG CAGCAATAAT AATCTTACAC TTTTTTCAAT
28801 TACAAAACAA TATACTGGTA CTTATTACAG TACAAACTTT CATACAGGAC AAGATAAATA
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Fig. 7H

SEQ ID NO: 3


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28861 TTATACTGTT AAGGTAGAAA ATCCTACCAC TCCTAGAACT ACCACCACCA CCACTACTGC
28921 AAAGCCCACT GTGAAAACTA CAACTAGGAC CACCACAACT ACAGAAACCA CCACCAGCAC
28981 AACACTTGCT GCAACTACAC ACACACACAC TAAGCTAACC TTACAGACCA CTAATGATTT
29041 GATCGCCCTG CTGCAAAAGG GGGATAACAG CACCACTTCC AATGAGGAGA TACCCAAATC
29101 CATGATTGGC ATTATTGTTG CTGTAGTGGT GTGCATGTTG ATCATCGCCT TGTGCATGGT
29161 GTACTATGCC TTCTGCTACA GAAAGCACAG ACTGAACGAC AAGCTGGAAC ACTTACTAAG
29221 TGTTGAATTT TAATTTTTTA GAACCATGAA GATCCTAGGC CTTTTTAGTT TTTCTATCAT
29281 TACCTCTGCT CTTTGTGAAT CAGTGGATAG AGATGTTACT ATTACCACTG GTTCTAATTA
29341 TACACTGAAA GGGCCACCCT CAGGTATGCT TTCGTGGTAT TGCTATTTTG GAACTGACAC
29401 TGATCAAACT GAATTATGCA ATTTTCAAAA AGGCAAAACC TCAAACTCTA AAATCTCTAA
29461 TTATCAATGC AATGGCACTG ATCTGATACT ACTCAATGTC ACGAAAGCAT ATGGTGGCAG
29521 TTATTATTGC CCTGGACAAA ACACTGAAGA AATGATTTTT TACAAAGTGG AAGTGGTTGA
29581 TCCCACTACA CCACCCACCA CCACAACTAT TCATACCACA CACACAGAAC AAACACCAGA
29641 GGCAACAGAA GCAGAGTTGG CCTTCCAGGT TCACGGAGAT TCCTTTGCTG TCAATACCCC
29701 TACACCCGAT CAGCGGTGTC CGGGGCCGCT AGTCAGCGGC ATTGTCGGTG TGCTTTCGGG
29761 ATTAGCAGTC ATAATCATCT GCATGTTCAT TTTTGCTTGC TGCTATAGAA GGCTTTACCG
29821 ACAAAAATCA GACCCACTGC TGAACCTCTA TGTTTAATTT TTTCCAGAGC CATGAAGGCA
29881 GTTAGCGCTC TAGTTTTTTG TTCTTTGATT GGCATTGTTT TTAATAGTAA AATTACCAGA
29941 GTTAGCTTTA TTAAACATGT TAATGTAACT GAAGGAGATA ACATCACACT AGCAGGTGTA
30001 GAAGGTGCTC AAAACACCAC CTGGACAAAA TACCATCTAG GATGGAGAGA TATTTGCACC
30061 TGGAATGTAA CTTATTATTG CATAGGAGTT AATCTTACCA TTGTTAACGC TAACCAATCT
30121 CAGAATGGGT TAATTAAAGG ACAGAGTGTT AGTGTGACCA GTGATGGGTA CTATACCCAG
30181 CATAGTTTTA ACTACAACAT TACTGTCATA CCACTGCCTA CGCCTAGCCC ACCTAGCACT
30241 ACCACACAGA CAACCACATA CAGTACATCA AATCAGCCTA CCACCACTAC AGCAGCAGAG
30301 GTTGCCAGCT CGTCTGGGGT CCGAGTGGCA TTTTTGATGT TGGCCCCATC TAGCAGTCCC
30361 ACTGCTAGTA CCAATGAGCA GACTACTGAA TTTTTGTCCA CTGTCGAGAG CCACACCACA
30421 GCTACCTCCA GTGCCTTCTC TAGCACCGCC AATCTCTCCT CGCTTTCCTC TACACCAATC
30481 AGCCCCGCTA CTACTCCTAG CCCCGCTCCT CTTCCCACTC CCCTGAAGCA AACAGACGGC
30541 GGCATGCAAT GGCAGATCAC CCTGCTCATT GTGATCGGGT TGGTCATCCT GGCCGTGTTG
30601 CTCTACTACA TCTTCTGCCG CCGCATTCCC AACGCGCACC GCAAGCCGGC CTACAAGCCC
30661 ATCGTTATCG GGCAGCCGGA GCCGCTTCAG GTGGAAGGGG GTCTAAGGAA TCTTCTCTTC
30721 TCTTTTACAG TATGGTGATT GAANTATGAT TCCTAGACAA TTCTTGATCA CTATTCTTAT
30781 CTGCCTCCTC CAAGTCTGTG CCACCCTCGC TCTGGTGGCC AACGCCAGTC CAGACTGTAT
30841 TGGGCCCTTC GCCTCCTACG TGCTCTTTGC CTTCGTCACC TGCATCTGCT GCTGTAGCAT
30901 AGTCTGCCTG CTTATCACCT TCTTCCAGTT CATTGACTGG ATCTTTGTGC GCATCGCCTA
30961 CCTGCGCCAC CACCCCCAGT ACCGCGACCA GCGAGTGGCG CAGCTGCTCA GGCTCCTCTG
31021 ATAAGCATGC GGGCTCTGCT ACTTNTCGCG CTTCTGCTGT TAGTGCTCCC CCGTCCCGTC
31081 GACCCCCGGT CCCCCACTCA GTCCCCCGAG GAGGTTCGCA AATGCAAATT CCAAGAACCC
31141 TGGAAATTCC TCAAATGCTA CCGCCAAAAA TCAGACATGC ATCCCAGCTG GATCATGATC
31201 ATTGGGATCG TGAACATTCT GGCCTGCACC CTCATCTCCT TTGTGATTTA CCCCTGCTTT
31261 GACTTTGGTT GGAACTCGCC AGAGGCGCTC TATCTCCCGC CTGAACCTGA CACACCACCA
31321 CAGCATCAAC CTCAGGCACA CGCACTACCA CCACCACAGC CTAGGCCACA ATACATGCCC
31381 ATATTAGACT ATGAGGCCGA GCCACAGCGA CCCATGCTCC CCGCTATTAG TTACTTCAAT
31441 CTAACCGGCG GAGATGACTG ACCCACTGGC CAATAACAAC GTCAACGACC TTCTCCTGGA
31501 CATGGACGGC CGCGCCTCGG AGCAGCGACT CGCCCAACTT CGCATTCGTC AGCAGCAGGA
31561 GAGAGCCGTC AAGGAGCTGC AGGACGGCAT AGCCATCCAC CAGTGCAAGA GAGGCATCTT
31621 CTGCCTGGTG AAACAGGCCA AGATCTCCTA CGAGGTCACC CAGACCGACC ATCGCCTCTC
31681 CTACGAGCTC CTGCAGCAGC GCCAGAAGTT CACCTGCCTG GTCGGAGTCA ACCCCATCGT
31741 CATCACCCAG CCAGCAGTCG GGCGATACCA AGGGGTGCAT CCACTGCTCC TGCGACTCCC
31801 CCGACTGCGT CCACACTCTG ATCAAGACCC TCTGCGGCCT CCGCGACCTC CTCCCCATGA
31861 ACTAATCACC CCCTTATCCA GTGAAATAAA GATCATATTG ATGATGATTT AAATAAAAAA
31921 AATAATCATT TGATTTGAAA TAAAGATACA ATCATATTGA TGATTTGAGT TTAACAAAAA
31981 TAAAGAATCA CTTACTTGAA ATCTGATACC AGGTCTCTGT CCATGTTTTC TGCCAACACC
32041 ACCTCACTCC CCTCTTCCCA GCTCTGGTAC TGCAGGCCCC GGCGGGCTGC AAACTTCCTC
32101 CACACGCTGA AGGGGATGTC AAATTCCTCC TGTCCCTCAA TCTTCATTTT ATCTTCTATC
32161 AGATGTCCAA AAAGCGCGTC CGGGTGGATG ATGACTTCGA CCCCGTCTAC CCCTACGATG
32221 CAGACAACGC ACCGACCGTG CCCTTCATCA ACCCCCCCTT CGTCTCTTCA GATGGATTCC
32281 AAGAGAAGCC CCTGGGGGTG TTGTCCCTGC GACTGGCTGA CCCCGTCACC ACCAAGAACG
32341 GGGAAATCAC CCTCAAGCTG GGAGAGGGGG TGGACCTCGA CTCGTCGGGA AAACTCATCT
32401 CCAACACGGC CACCAAGGCC GCCGCCCCTC TCAGTATTTC AAACAACACC ATTTCCCTTA
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Fig. 7I

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32461 AAACTGCTGC CCCTTTCTAC AACAACAATG GAACTTTAAG CCTCAATGTC TCCACACCAT
32521 TAGCAGTATT TCCCACATTT AACACTTTAG GCATAAGTCT TGGAAACGGT CTTCAGACTT
32581 CAAATAAGTT GTTGACTGTA CAACTAACTC ATCCTCTTAC ATTCAGCTCA AATAGCATCA
32641 CAGTAAAAAC AGACAAAGGG CTATATATTA ACTCCAGTGG AAACAGAGGA CTTGAGGCTA
32701 ATATAAGCCT AAAAAGAGGA CTAGTTTTTG ACGGTAATGC TATTGCAACA TATATTGGAA
32761 ATGGCTTAGA CTATGGATCT TATGATAGTG ATGGAAAAAC AAGACCCGTA ATTACCAAAA
32821 TTGGAGCAGG ATTAAATTTT GATGCTAACA AAGCAATAGC TGTCAAACTA GGCACAGGTT
32881 TAAGTTTTGA CTCCGCTGGT GCCTTGACAG CTGGAAACAA ACAGGATGAC AAGCTAACAC
32941 TTTGGACTAC CCCTGACCCA AGCCCTAATT GTCAATTACT TTCAGACAGA GATGCCAAAT
33001 TTACTCTCTG TCTTACAAAA TGCGGTAGTC AAATACTAGG CACTGTGGCA GTGGCGGCTG
33061 TTACTGTAGG ATCAGCACTA AATCCAATTA ATGACACAGT CAAAAGCGCC ATAGTTTTCC
33121 TTAGATTTGA TTCCGATGGT GTACTCATGT CAAACTCATC AATGGTAGGT GATTACTGGA
33181 ACTTTAGGGA GGGACAGACC ACTCAAAGTG TAGCCTATAC AAATGCTGTG GGATTCATGC
33241 CAAATATAGG TGCATATCCA AAAACCCAAA GTAAAACACC TAAAAATAGC ATAGTCAGTC
33301 AGGTATATTT AACTGGAGAA ACTACTATGC CAATGACACT AACCATAACT TTCAATGGCA
33361 CTGATGAAAA AGACACAACC CCAGTTAGCA CCTACTCTAT GACTTTTACA TGGCAGTGGA
33421 CTGGAGACTA TAAGGACAAA AATATTACCT TTGCTACCAA CTCATTCTCT TTTTCCTACA
33481 TCGCCCAGGA ATAATCCCAC CCAGCAAGCC AACCCCTTTT CCCACCACCT TTGTCTATAT
33541 GGAAACTCTG AAACAGAAAA ATAAAGTTCA AGTGTTTTAT TGAATCAACA GTTTTACAGG
33601 ACTCGAGCAG TTATTTTTCC TCCACCCTCC CAGGACATGG AATACACCAC CCTCTCCCCC
33661 CGCACAGCCT TGAACATCTG AATGCCATTG GTGATGGACA TGCTTTTGGT CTCCACGTTC
33721 CACACAGTTT CAGAGCGAGC CAGTCTCGGA TCGGTCAGGG AGATGAAACC CTCCGGGCAC
33781 TCCCGCATCT GCACCTCACA GCTCAACAGC TGAGGATTGT CCTCGGTGGT CGGGATCACG
33841 GTTATCTGGA AGAAGCAGAA GAGCGGCGGT GGGAATCATA GTCCGCGAAC GGGATCGGCC
33901 GGTGGTGTCG CATCAGGCCC CGCAGCAGTC GCTGCCGCCG CCGCTCCGTC AAGCTGCTGC
33961 TCAGGGGGTT CGGGTCCAGG GACTCCCTCA GCATGATGCC CACGGCCCTC AGCATCAGTC
34021 GTCTGGTGCG GCGGGCGCAG CAGCGCATGC GAATCTCGCT CAGGTCACTG CAGTACGTGC
34081 AACACAGGAC CACCAGGTTG TTCAACAGTC CATAGTTCAA CACGCTCCAG CCGAAACTCA
34141 TCGCGGGAAG GATGCTACCC ACGTGGCCGT CGTACCAGAT CCTCAGGTAA ATCAAGTGGC
34201 GCTCCCTCCA GAAGACGCTG CCCATGTACA TGATCTCCTT GGGCATGTGG CGGTTCACCA
34261 CCTCCCGGTA CCACATCACC CTCTGGTTGA ACATGCAGCC CCGGATGATC CTGCGGAACC
34321 ACAGGGCCAG CACCGCCCCG CCCGCCATGC AGCGAAGAGA CCCCGGATCC CGGCAATGAC
34381 AATGGAGGAC CCACCGCTCG TACCCGTGGA TCATCTGGGA GCTGAACAAG TCTATGTTGG
34441 CACAGCACAG GCATATGCTC ATGCATCTCT TCAGCACTCT CAGCTCCTCG GGGGTCAAAA
34501 CCATATCCCA GGGCACGGGG AACTCTTGCA GGACAGCGAA CCCCGCAGAA CAGGGCAATC
34561 CTCGCACATA ACTTACATTG TGCATGGACA GGGTATCGCA ATCAGGCAGC ACCGGGTGAT
34621 CCTCCACCAG AGAAGCGCGG GTCTCGGTCT CCTCACAGCG TGGTAAGGGG GCCGGCCGAT
34681 ACGGGTGATG GCGGGACGCG GCTGATCGTG TTCTCGACCG TGTCATGATG CAGTTGCTTT
34741 CGGACATTTT CGTACTTGCT GTAGCAGAAC CTGGTCCGGG CGCTGCACAC CGATCGCCGG
34801 CGGCGGTCTC GGCGCTTGGA ACGCTCGGTG TTAAAGTTGT AAAACAGCCA CTCTCTCAGA
34861 CCGTGCAGCA GATCTAGGGC CTCAGGAGTG ATGAAGATCC CATCATGCCT GATAGCTCTG
34921 ATCACATCGA CCACCGTGGA ATGGGCCAGG CCCAGCCAGA TGATGCAATT TTGTTGGGTT
34981 TCGGTGACGG CGGGGGAGGG AAGAACAGGA AGAACCATGA TTAACTTTTA ATCCAAACGG
35041 TCTCGGAGCA CTTCAAAATG AAGGTCACGG AGATGGCACC TCTCGCCCCC GCTGTGTTGG
35101 TGGAAAATAA CAGCCAGGTC AAAGGTGATA CGGTTCTCGA GATGTTCCAC GGTGGCTTCC
35161 AGCAAAGCCT CCACGCGCAC ATCAGAAACA AGACAATAGC GAAAGCGGGA GGGTTCTCTA
35221 ATTCCTCAAC CATCATGTTA CACTCCTGCA CCATCCCCAG ATAATTTTCA TTTTTCCAGC
35281 CTTGAATGAT TCGAACTAGT TCCTGAGGTA AATCCAAGCC AGCCATGATA AAAAGCTCGC
35341 GCAGAGCACC CTCCACCGGC ATTCTTAAGC ACACCCTCAT AATTCCAAGA TATTCTGCTC
35401 CTGGTTCACC TGCAGCAGAT TGACAAGCGG AATATCAAAA TCTCTGCCGC GATCCCTGAG
35461 CTCCTCCCTC AGCAATAACT GTAAGTACTC TTTCATATCG TCTCCGAAAT TTTTAGCCAT
35521 AGGACCCCCA GGAATAAGAG AAGGGCAAGC CACATTACAG ATAAACCGAA GTCCCCCCCA
35581 GTGAGCATTG CCAAATGTAA GATTGAAATA AGCATGCTGG CTAGACCCGG TGATATCTTC
35641 CAGATAACTG GACAGAAAAT CGGGTAAGCA ATTTTTAAGA AAATCAACAA AAGAAAAATC
35701 TTCCAGGTGC ACGTTTAGGG CCTCGGGAAC AACGATGGAG TAAGTGCAAG GGGTGCGTTC
35761 CAGCATGGTT AGTTAGCTGA TCTGTAAAAA AACAAAAAAT AAAACATTAA ACCATGCTAG
35821 CCTGGCGAAC AGGTGGGTAA ATCGTTCTCT CCAGCACCAG GCAGGCCACG GGGTCTCCGG
35881 CGCGACCCTC GTAAAAATTG TCGCTATGAT TGAAAACCAT CACAGAGAGA CGTTCCCGGT
35941 GGCCGGCGTG AATGATTCGA GAAGAAGCAT ACACCCCCCG GAACATTGGA GTCCGTGAGT
36001 GAAAAAAAGC GGCCGAGGAA GCAATGAGGC ACTACAACGC TCACTCTCAA GTCCAGCAAA
```

Fig. 7J

SEQ ID NO: 3


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36061 GCGATGCCAT GCGGATGAAG CACAAAATTT TCAGGTGCGT AAAAAATGTA ATTACTCCCC
36121 TCCTGCACAG GCAGCGAAGC TCCCGATCCC TCCAGATACA CATACAAAGC CTCAGCGTCC
36181 ATAGCTTACC GAGCGGCAGC AGCAGCGGCA CACAACAGGC GCAAGAGTCA GAGAAAAGAC
36241 TGAGCTCTAA CCTGTCCGCC CGCTCTCTGC TCAATATATA GCCCCAGATC TACACTGACG
36301 TAAAGGCCAA AGTCTAAAAA TACCCGCCAA ATAATCACAC ACGCCCAGCA CACGCCCAGA
36361 AACCGGTGAC ACACTCAGAA AAATACGCGC ACTTCCTCAA ACGGCCAAAC TGCCGTCATT
36421 TCCGGGTTCC CACGCTACGT CATCAAAACA CGACTTTCAA ATTCCGTCGA CCGTTAAAAA
36481 CATCACCCGC CCCGCCCCTA ACGGTCGCCG CTCCCGCAGC CAATCACCTT CCTCCCTCCC
36541 CAAATTCAAA CAGCTCATTT GCATATTAAC GCGCACCAAA AGTTTGAGGT ATATTATTGA
36601 TGATGG
```

Fig. 7K

SEQ ID No: 4


```
   1 CATCATCAAT AATATACCTC AAACTTTTGG TGCGCGTTAA TATGCAAATG AGCTGTTTGA
  61 ATTTGGGGAG GGAGGAAGGT GATTGGCCGA GAGACGGGCG ACCGTTAGGG GCGGGGCGGG
 121 TGACGTTTTG ATGACGTGGC CGTGAGGCGG AGCCGGTTTG CAAGTTCTCG TGGGAAAAGT
 181 GACGTCAAAC GAGGTGTGGT TTGAACACGG AAATACTCAA TTTTCCCGCG CTCTCTGACA
 241 GGAAATGAGG TGTTTCTGGG CGGATGCAAG TGAAAACGGG CCATTTTCGC GCGAAAACTG
 301 AATGAGGAAG TGAAAATCTG AGTAATTTCG CGTTTATGGC AGGGAGGAGT ATTTGCCGAG
 361 GGCCGAGTAG ACTTTGACCG ATTACGTGGG GGTTTCGATT ACCGTATTTT TCACCTAAAT
 421 TTCCGCGTAC GGTGTCAAAG TCCGGTGTTT TTACGTAGGC GTCAGCTGAT CGCCAGGGTA
 481 TTTAAACCTG CGCTCTCTAG TCAAGAGGCC ACTCTTGAGT GCCAGCGAGT AGAGTTTTCT
 541 CCTCCGCGCC GCGAGTCAGA TCTACACTTT GAAAGATGAG GCACCTGAGA GACCTGCCCG
 601 GTAATGTTTT CCTGGCTACT GGGAACGAGA TTCTGGAATT GGTGGTGGAC GCCATGATGG
 661 GTGGCGACCC TCCTGAGCCC CCTACCCCAT TTGAGGCGCC TTCGCTGTAC GATTTGTATG
 721 ATCTGGAGGT GGATGTGCCC GAGAACGACC CCAACGAGGA GGCGGTGAAT GATTTGTTTA
 781 GCGATGCCGC GCTGCTGGCT GCCGAGCAGG CTAATACGGA CTCTGGCTCA GACAGCGATT
 841 CCTCTCTCCA TACCCCGAGA CCCGGCAGAG GTGAGAAAAA GATCCCCGAG CTTAAAGGGG
 901 AAGAGCTCGA CCTGCGCTGC TATGAGGAAT GCTTGCCTCC GAGCGATGAT GAGGAGGACG
 961 AGGAGGCGAT TCGAGCTGCA TCGAACCAGG GAGTGAAAGC TGCGGGCGAA AGCTTTAGCC
1021 TGGACTGTCC TACTCTGCCC GGACACGGCT GTAAGTCTTG TGAATTTCAT CGCATGAATA
1081 CTGGAGATAA GAATGTGATG TGTGCCCTGT GCTATATGAG AGCTTACAAC CATTGTGTTT
1141 ACAGTAAGTG TGATTAACTT TAGTTGGGAA GGCAGAGGGT GACTGGGTGC TGACTGGTTT
1201 ATTTATGTAT ATGTTTTTTT ATGTGTAGGT CCCGTCTCTG ACGTAGATGA GACCCCCACT
1261 TCAGAGTGCA TTTCATCACC CCCAGAAATT GGCGAGGAAC CGCCCGAAGA TATTATTCAT
1321 AGACCAGTTG CAGTGAGAGT CACCGGGCGG AGAGCAGCTG TGGAGAGTTT GGATGACTTG
1381 CTACAGGGTG GGGATGAACC TTTGGACTTG TGTACCCGGA AACGCCCCAG GCACTAAGTG
1441 CCACACATGT GTGTTTACTT AAGGTGATGT CAGTATTTAT AGGGTGTGGA GTGCAATAAA
1501 ATCCGTGTTG ACTTTAAGTG CGTGGTTTAT GACTCAGGGG TGGGGACTGT GGGTATATAA
1561 GCAGGTGCAG ACCTGTGTGG TCAGTTCAGA GCAGGACTCA TGGAGATCTG GACGGTCTTG
1621 GAAGACTTTC ACCAGACTAG ACAGCTGCTA GAGAACTCAT CGGAGGGGGT CTCTTACCTG
1681 TGGAGATTCT GCTTCGGTGG GCCTCTAGCT AAGCTAGTCT ATAGGGCCAA ACAGGATTAT
1741 AAGGATCAAT TTGAGGATAT TTTGAGAGAG TGTCCTGGTA TTTTTGACTC TCTCAACTTG
1801 GGCCATCAGT CTCACTTTAA CCAGAGTATT CTGAGAGCCC TTGACTTTTC TACTCCTGGC
1861 AGAACTACCG CCGCGGTAGC CTTTTTTGCC TTTATCCTTG ACAAATGGAG TCAAGAAACC
1921 CATTTCAGCA GGGATTACCG TCTGGACTGC TTAGCAGTAG CTTTGTGGAG AACATGGAGG
1981 TGCCAGCGCC TGAATGCAAT CTCCGGCTAC TTGCCAGTAC AGCCGGTAGA CACGCTGAGG
2041 ATCCTGAGTC TCCAGTCACC CCAGGAACAC CAACGCCGCC AGCAGCCGCA GCAGGAGCAG
2101 CAGCAAGAGG AGGAGGAGGA TCGAGAAGAG AACCCGAGAG CCGGTCTGGA CCCTCCGGTG
2161 GCGGAGGAGG AGGAGTAGCT GACTTGTTTC CCGAGCTGCG CCGGGTGCTG ACTAGGTCTT
2221 CCAGTGGACG GGAGAGGGGG ATTAAGCGGG AGAGGCATGA GGAGACTAGC CACAGAACTG
2281 AACTGACTGT CAGTCTGATG AGCCGCAGGC GCCCAGAATC GGTGTGGTGG CATGAGGTTC
2341 AGTCGCAGGG GATAGATGAG GTCTCGGTGA TGCATGAGAA ATATTCCCTG GAACAAGTCA
2401 AGACTTGTTG GTTGGAGCCT GAGGATGATT GGGAGGTAGC CATCAGGAAT TATGCCAAGC
2461 TGGCTCTGAA GCCAGACAAG AAGTACAAGA TTACCAAACT GATTAATATC AGAAATTCCT
2521 GCTACATTTC AGGGAATGGG GCCGAGGTGG AGATCAGTAC CCAGGAGAGG GTGGCCTTCA
2581 GATGTTGTAT GATGAATATG TACCCGGGGG TGGTGGGCAT GGAGGGAGTC ACCTTTATGA
2641 ACGCGAGGTT CAGGGGTGAT GGGTATAATG GGGTGGTCTT TATGGCCAAC ACCAAGCTGA
2701 CAGTGCACGG ATGCTCCTTC TTTGGGTTCA ATAACATGTG CATCGAGGCC TGGGGCAGTG
2761 TTTCAGTGAG GGGATGCAGC TTTTCAGCCA ACTGGATGGG GGTCGTGGGC AGAACCAAGA
2821 GCAAGGTGTC AGTGAAGAAA TGCCTGTTCG AGAGGTGCCA CCTGGGGGTG ATGAGCGAGG
2881 GCGAAGCCAA AGTCAAACAC TGCGCCTCTA CTGAGACGGG CTGCTTTGTG CTGATCAAGG
2941 GCAATGCCCA AGTCAAGCAT AACATGATCT GTGGGGCCTC GGATGAGCGC GGCTACCAGA
3001 TGCTGACCTG CGCCGGTGGG AACAGCCATA TGCTGGCCAC CGTGCATGTG ACCTCGCACC
3061 CCCGCAAGAC ATGGCCCGAG TTCGAGCACA ACGTCATGAC CCGATGCAAT GTGCACCTGG
3121 GGTCCCGCCG AGGCATGTTC ATGCCCTACC AGTGCAACAT GCAATTTGTG AAGGTGCTGC
3181 TGGAGCCCGA TGCCATGTCC AGAGTGAGCC TGACGGGGGT GTTTGACATG AATGTGGAGC
3241 TGTGGAAAAT TCTGAGATAT GATGAATCCA AGACCAGGTG CCGGGCCTGC GAATGCGGAG
3301 GCAAGCACGC CAGGCTTCAG CCCGTGTGTG TGGAGGTGAC GGAGGACCTG CGACCCGATC
3361 ATTTGGTGTT GTCCTGCAAC GGGACGGAGT TCGGCTCCAG CGGGGAAGAA TCTGACTAGA
3421 GTGAGTAGTG TTTGGGGGAG GTGGAGGGCT TGTATGAGGG GCAGAATGAC TAAAATCTGT
3481 GTTTTTCTGT GTGTTGCAGC AGCATGAGCG GAAGCGCCTC CTTTGAGGGA GGGGTATTCA
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Fig. 8A

SEQ ID No: 4

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3541 GCCCTTATCT GACGGGGCGT CTCCCCTCCT GGGCGGGAGT GCGTCAGAAT GTGATGGGAT
3601 CCACGGTGGA CGGCCGGCCC GTGCAGCCCG CGAACTCTTC AACCCTGACC TACGCGACCC
3661 TGAGCTCCTC GTCCGTGGAC GCAGCTGCCG CCGCAGCTGC TGCTTCCGCC GCCAGCGCCG
3721 TGCGCGGAAT GGCCCTGGGC GCCGGCTACT ACAGCTCTCT GGTGGCCAAC TCGACTTCCA
3781 CCAATAATCC CGCCAGCCTG AACGAGGAGA AGCTGCTGCT GCTGATGGCC CAGCTCGAGG
3841 CCCTGACCCA GCGCCTGGGC GAGCTGACCC AGCAGGTGGC TCAGCTGCAG GCGGAGACGC
3901 GGGCCGCGGT TGCCACGGTG AAAACCAAAT AAAAAATGAA TCAATAAATA AACGGAGACG
3961 GTTGTTGATT TTAACACAGA GTCTTGAATC TTTATTTGAT TTTTCGCGCG CGGTAGGCCC
4021 TGGACCACCG GTCTCGATCA TTGAGCACCC GGTGGATTTT TTCCAGGACC CGGTAGAGGT
4081 GGGCTTGGAT GTTGAGGTAC ATGGGCATGA GCCCGTCCCG GGGGTGGAGG TAGCTCCATT
4141 GCAGGGCCTC GTGCTCGGGG GTGGTGTTGT AAATCACCCA GTCATAGCAG GGGCGCAGGG
4201 CGTGGTGCTG CACGATGTCC TTGAGGAGGA GACTGATGGC CACGGGCAGC CCCTTGGTGT
4261 AGGTGTTGAC GAACCTGTTG AGCTGGGAGG GATGCATGCG GGGGGAGATG AGATGCATCT
4321 TGGCCTGGAT CTTGAGATTG GCGATGTTCC CGCCCAGATC CCGCCGGGGG TTCATGTTGT
4381 GCAGGACCAC CAGCACGGTG TATCCGGTGC ACTTGGGGAA TTTGTCATGC AACTTGGAAG
4441 GGAAGGCGTG AAAGAATTTG GAGACGCCCT TGTGACCGCC CAGGTTTTCC ATGCACTCAT
4501 CCATGATGAT GGCGATGGGC CCGTGGGCGG CGGCCTGGGC AAAGACGTTT CGGGGGTCGG
4561 ACACATCGTA GTTGTGGTCC TGGGTGAGCT CGTCATAGGC CATTTTAATG AATTTGGGGC
4621 GGAGGGTGCC CGACTGGGGG ACGAAGGTGC CCTCGATCCC GGGGGCGTAG TTGCCCTCGC
4681 AGATCTGCAT CTCCCAGGCC TTGAGCTCGG AGGGGGGGAT CATGTCCACC TGCGGGGCGA
4741 TGAAAAAAAC GGTTTCCGGG GCGGGGGAGA TGAGCTGGGC CGAAAGCAGG TTCCGGAGCA
4801 GCTGGGACTT GCCGCAGCCG GTGGGGCCGT AGATGACCCC GATGACCGGC TGCAGGTGGT
4861 AGTTGAGGGA GAGACAGCTG CCGTCCTCGC GGAGGAGGGG GGCCACCTCG TTCATCATCT
4921 CGCGCACATG CATGTTCTCG CGCACGAGTT CCGCCAGGAG GCGCTCGCCC CCCAGCGAGA
4981 GGAGCTCTTG CAGCGAGGCG AAGTTTTTCA GCGGCTTGAG CCCGTCGGCC ATGGGCATTT
5041 TGGAGAGGGT CTGTTGCAAG AGTTCCAGAC GGTCCCAGAG CTCGGTGATG TGCTCTAGGG
5101 CATCTCGATC CAGCAGACCT CCTCGTTTCG CGGGTTGGGG CGACTGCGGG AGTAGGGCAC
5161 CAGGCGATGG GCGTCCAGCG AGGCCAGGGT CCGGTCCTTC CAGGGTCGCA GGGTCCGCGT
5221 CAGCGTGGTC TCCGTCACGG TGAAGGGGTG CGCGCCGGGC TGGGCGCTTG CGAGGGTGCG
5281 CTTCAGGCTC ATCCGGCTGG TCGAGAACCG CTCCCGGTCG GCGCCCTGCG CGTCGGCCAG
5341 GTAGCAATTG AGCATGAGTT CGTAGTTGAG CGCCTCGGCC GCGTGGCCCT TGGCGCGGAG
5401 CTTACCTTTG GAAGTGTGTC CGCAGACGGG ACAGAGGAGG GACTTGAGGG CGTAGAGCTT
5461 GGGGGCGAGG AAGACGGACT CGGGGGCGTA GGCGTCCGCG CCGCAGCTGG CGCAGACGGT
5521 CTCGCACTCC ACGAGCCAGG TGAGGTCGGG CCGGTTGGGG TCAAAAACGA GGTTTCCTCC
5581 GTGCTTTTTG ATGCGTTTCT TACCTCTGGT CTCCATGAGC TCGTGTCCCC GCTGGGTGAC
5641 AAAGAGGCTG TCCGTGTCCC CGTAGACCGA CTTTATGGGC CGGTCCTCGA GCGGGGTGCC
5701 GCGGTCCTCG TCGTAGAGGA ACCCCGCCCA CTCCGAGACG AAGGCCCGGG TCCAGGCCAG
5761 CACGAAGGAG GCCACGTGGG AGGGGTAGCG GTCGTTGTCC ACCAGCGGGT CCACCTTCTC
5821 CAGGGTATGC AAGCACATGT CCCCCTCGTC CACATCCAGG AAGGTGATTG GCTTGTAAGT
5881 GTAGGCCACG TGACCGGGGG TCCCGGCCGG GGGGGTATAA AAGGGGGCGG GCCCCTGCTC
5941 GTCCTCACTG TCTTCCGGAT CGCTGTCCAG GAGCGCCAGC TGTTGGGGTA GGTATTCCCT
6001 CTCGAAGGCT GGCATAACCT CGGCACTCAG GTTGTCAGTT TCTAGAAACG AGGAGGATTT
6061 GATATTGACG GTGCCGTTGG AGACGCCTTT CATGAGCCCC TCGTCCATCT GGTCAGAAAA
6121 GACGATCTTT TTGTTGTCGA GCTTGGTGGC GAAGGAGCCG TAGAGGGCGT TGGAGAGGAG
6181 CTTGGCGATG GAGCGCATGG TCTGGTTCTT TTCCTTGTCG GCGCGCTCCT TGGCGGCGAT
6241 GTTGAGCTGC ACGTACTCGC GCGCCACGCA CTTCCATTCG GGGAAGACGG TGGTGAGCTC
6301 GTCGGGCACG ATTCTGACCC GCCAGCCGCG GTTGTGCAGG GTGATGAGGT CCACGCTGGT
6361 GGCCACCTCG CCGCGCAGGG GCTCGTTGGT CCAGCAGAGG CGCCCGCCCT TGCGCGAGCA
6421 GAAGGGGGGC AGCGGGTCCA GCATGAGCTC GTCGGGGGGG TCGGCGTCCA CGGTGAAGAT
6481 GCCGGGCAGA AGCTCGGGGT CGAAGTAGCT GATGCAGGTG TCCAGATCGT CCAGCGCCGC
6541 TTGCCAGTCG CGCACGGCCA GCGCGCGCTC GTAGGGGCTG AGGGGCGTGC CCCAGGGCAT
6601 GGGGTGCGTG AGCGCGGAGG CGTACATGCC GCAGATGTCG TAGACGTAGA GGGGCTCCTC
6661 GAGGACGCCG ATGTAGGTGG GGTAGCAGCG CCCCCCGCGG ATGCTGGCGC GCACGTAGTC
6721 GTACAGCTCG TGCGAGGGCG CGAGGAGCCC CGTGCCGAGG TTGGAGCGTT GCGGCTTTTC
6781 GGCGCGGTAG ACGATCTGGC GGAAGATGGC GTGGGAGTTG GAGGAGATGG TGGGCCTCTG
6841 GAAGATGTTG AAGTGGGCGT GGGGCAGGCC GACCGAGTCC CTGATGAAGT GGGCGTAGGA
6901 GTCCTGCAGC TTGGCGACGA GCTCGGCGGT GACGAGGACG TCCAGGGCGC AGTAGTCGAG
6961 GGTCTCTTGG ATGATGTCGT ACTTGAGCTG GCCCTTCTGC TTCCACAGCT CGCGGTTGAG
7021 AAGGAACTCT TCGCGGTCCT TCCAGTACTC TTCGAGGGGG AACCCGTCCT GATCGGCACG
7081 GTAAGAGCCC ACCATGTAGA ACTGGTTGAC GGCCTTGTAG GCGCAGCAGC CCTTCTCCAC
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Fig. 8B

SEQ ID No: 4

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7141 GGGGAGGGCG TAAGCTTGTG CGGCCTTGCG CAGGGAGGTG TGGGTGAGGG CGAAGGTGTC
7201 GCGCACCATG ACCTTGAGGA ACTGGTGCTT GAAGTCGAGG TCGTCGCAGC CGCCCTGCTC
7261 CCAGAGCTGG AAGTCCGTGC GCTTCTTGTA GGCGGGGTTG GGCAAAGCGA AAGTAACATC
7321 GTTGAAGAGG ATCTTGCCCG CGCGGGGCAT GAAGTTGCGA GTGATGCGGA AAGGCTGGGG
7381 CACCTCGGCC CGGTTGTTGA TGACCTGGGC GGCGAGGACG ATCTCGTCGA AGCCGTTGAT
7441 GTTGTGCCCG ACGATGTAGA GTTCCACGAA TCGCGGGCGG CCCTTAACGT GGGGCAGCTT
7501 CTTGAGCTCG TCGTAGGTGA GCTCGGCGGG GTCGCTGAGC CCGTGCTGCT CGAGGGCCCA
7561 GTCGGCGACG TGGGGGTTGG CGCTGAGGAA GGAAGTCCAG AGATCCACGG CCAGGGCGGT
7621 CTGCAAGCGG TCCCGGTACT GACGGAACTG CTGGCCCACG GCCATTTTTT CGGGGGTGAC
7681 GCAGTAGAAG GTGCGGGGGT CGCCGTGCCA GCGGTCCCAC TTGAGCTGGA GGGCGAGGTC
7741 GTGGGCGAGC TCGACGAGCG GCGGGTCCCC GGAGAGTTTC ATGACCAGCA TGAAGGGGAC
7801 GAGCTGCTTG CCGAAGGACC CCATCCAGGT GTAGGTTTCC ACATCGTAGG TGAGGAAGAG
7861 CCTTTCGGTG CGAGGATGCG AGCCGATGGG GAAGAACTGG ATCTCCTGCC ACCAGTTGGA
7921 GGAATGGCTG TTGATGTGAT GGAAGTAGAA ATGCCGACGG CGCGCCGAGC ACTCGTGCTT
7981 GTGTTTATAC AAGCGTCCGC AGTGCTCGCA ACGCTGCACG GGATGCACGT GCTGCACGAG
8041 CTGTACCTGG GTTCCTTTGA CGAGGAATTT CAGTGGGCAG TGGAGCGCTG GCGGCTGCAT
8101 CTGGTGCTGT ACTACGTCCT GGCCATCGGC GTGGCCATCG TCTGCCTCGA TGGTGGTCAT
8161 GCTGACGAGC CCGCGCGGGA GGCAGGTCCA GACTTCGGCT CGGACGGGTC GGAGAGCGAG
8221 GACGAGGGCG CGCAGGCCGG AGCTGTCCAG GGTCCTGAGA CGCTGCGGAG TCAGGTCAGT
8281 GGGCAGCGGC GGCGCGCGGT TGACTTGCAG GAGCTTTTCC AGGGCGCGCG GGAGGTCCAG
8341 ATGGTACTTG ATCTCCACGG CGCCGTTGGT GGCGACGTCC ACGGCTTGCA GGGTCCCGTG
8401 CCCCTGGGGC GCCACCACCG TGCCCCGTTT CTTCTTGGGC GCTGCTTCCA TGCCGGTCAG
8461 AAGCGGCGGC GAGGACGCGC GCCGGGCGGC AGGGGCGGCT CGGGACCCGG AGGCAGGGGC
8521 GGCAGGGGCA CGTCGGCGCC GCGCGCGGGC AGGTTCTGGT ACTGCGCCCG GAGAAGACTG
8581 GCGTGAGCGA CGACGCGACG GTTGACGTCC TGGATCTGAC GCCTCTGGGT GAAGGCCACG
8641 GGACCCGTGA GTTTGAACCT GAAAGAGAGT TCGACAGAAT CAATCTCGGT ATCGTTGACG
8701 GCGGCCTGCC GCAGGATCTC TTGCACGTCG CCCGAGTTGT CCTGGTAGGC GATCTCGGTC
8761 ATGAACTGCT CGATCTCCTC CTCCTGAAGG TCTCCGCGGC CGGCGCGCTC GACGGTGGCC
8821 GCGAGGTCGT TGGAGATGCG GCCCATGAGC TGCGAGAAGG CGTTCATGCC GGCCTCGTTC
8881 CAGACGCGGC TGTAGACCAC GGCTCCGTCG GGGTCGCGCG CGCGCATGAC CACCTGGGCG
8941 AGGTTGAGCT CGACGTGGCG CGTGAAGACC GCGTAGTTGC AGAGGCGCTG GTAGAGGTAG
9001 TTGAGCGTGG TGGCGATGTG CTCGGTGACG AAGAAGTACA TGATCCAGCG GCGGAGCGGC
9061 ATCTCGCTGA CGTCGCCCAG GGCTTCCAAG CGCTCCATGG CCTCGTAGAA GTCCACGGCG
9121 AAGTTGAAAA ACTGGGAGTT GCGCGCCGAG ACGGTCAACT CCTCCTCCAG AAGACGGATG
9181 AGCTCAGCGA TGGTGGCGCG CACCTCGCGC TCGAAGGCCC CGGGGGGCTC CTCTTCTTCC
9241 ATCTCTTCCT CCTCCACTAA CATCTCTTCT ACTTCCTCCT CAGGAGGCGG CGGCGGGGGA
9301 GGGGCCCTGC GTCGCCGGCG GCGCACGGGC AGACGGTCGA TGAAGCGCTC GATGGTCTCC
9361 CCGCGCCGGC GACGCATGGT CTCGGTGACG GCGCGCCCGT CCTCGCGGGG CCGCAGCGTG
9421 AAGACGCCGC CGCGCATCTC CAGGTGGCCG CCGGGGGGGT CTCCGTTGGG CAGGGAGAGG
9481 GCGCTGACGA TGCATCTTAT CAATTGGCCC GTAGGGACTC CGCGCAAGGA CCTGAGCGTC
9541 TCGAGATCCA CGGGATCCGA AAACCGCTGA ACGAAGGCTT CGAGCCAGTC GCAGTCGCAA
9601 GGTAGGCTGA GCCCGGTTTC TTGTTCTTCG GGGATTTCGG GAGGCGGGCG GGCGATGCTG
9661 CTGGTGATGA AGTTGAAGTA GGCGGTCCTG AGACGGCGGA TGGTGGCGAG GAGCACCAGG
9721 TCCTTGGGCC CGGCTTGCTG GATGCGCAGA CGGTCGGCCA TGCCCCAGGC GTGGTCCTGA
9781 CACCTGGCGA GGTCCTTGTA GTAGTCCTGC ATGAGCCGCT CCACGGGCAC CTCCTCCTCG
9841 CCCGCGCGGC CGTGCATGCG CGTGAGCCCG AACCCGCGCT GGGGCTGGAC GAGCGCCAGG
9901 TCGGCGACGA CGCGCTCGGC GAGGATGGCC TGCTGTATCT GGGTGAGGGT GGTCTGGAAG
9961 TCGTCGAAGT CGACGAAGCG GTGGTAGGCT CCGGTGTTGA TGGTATAGGA GCAGTTGGCC
10021 ATGACGGACC AGTTGACGGT CTGGTGGCCG GGTCGCACGA GCTCGTGGTA CTTGAGGCGC
10081 GAGTAGGCGC GCGTGTCGAA GATGTAGTCG TTGCAGGTGC GCACGAGGTA CTGGTATCCG
10141 ACGAGGAAGT GCGGCGGCGG CTGGCGGTAG AGCGGCCATC GCTCGGTGGC GGGGGCGCCG
10201 GGCGCGAGGT CCTCGAGCAT GAGGCGGTGG TAGCCGTAGA TGTACCTGGA CATCCAGGTG
10261 ATGCCGGCGG CGGTGGTGGA GGCGCGCGGG AACTCGCGGA CGCGGTTCCA GATGTTGCGC
10321 AGCGGCAGGA AGTAGTTCAT GGTGGCCGCG GTCTGGCCCG TGAGGCGCGC GCAGTCGTGG
10381 ATGCTCTAGA CATACGGGCA AAAACGAAAG CGGTCAGCGG CTCGACTCCG TGGCCTGGAG
10441 GCTAAGCGAA CGGGTTGGGC TGCGCGTGTA CCCCGGTTCG AATCTCGAAT CAGGCTGGAG
10501 CCGCAGCTAA CGTGGTACTG GCACTCCCGT CTCGACCCAA GCCTGCTAAC GAAACCTCCA
10561 GGATACGGAG GCGGGTCGTT TTTTGGCCTT GGTCGCTGGT CATGAAAAAC TAGTAAGCGC
10621 GGAAAGCGAC CGCCCGCGAT GGCTCGCTGC CGTAGTCTGG AGAAAGAATC GCCAGGGTTG
10681 CGTTGCGGTG TGCCCCGGTT CGAGCCTCAG CGCTCGGCGC CGGCCGGATT CCGCGGCTAA
```

Fig. 8C

SEQ ID No: 4

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10741 CGTGGGCGTG GCTGCCCCGT CGTTTCCAAG ACCCCTTAGC CAGCCGACTT CTCCAGTTAC
10801 GGAGCGAGCC CCTCTTTTTC TTGTGTTTTT GCCAGATGCA TCCCGTACTG CGGCAGATGC
10861 GCCCCCACCC TCCACCTCAA CCGCCCCTAC CGCCGCAGCA GCAGCAACAG CCGGCGCTTC
10921 TGCCCCCGCC CCAGCAGCAG CCAGCCACTA CCGCGGCGGC CGCCGTGAGC GGAGCCGGCG
10981 TTCAGTATGA CCTGGCCTTG GAAGAGGGCG AGGGGCTGGC GCGGCTGGGG GCGTCGTCGC
11041 CGGAGCGGCA CCCGCGCGTG CAGATGAAAA GGGACGCTCG CGAGGCCTAC GTGCCCAAGC
11101 AGAACCTGTT CAGAGACAGG AGCGGCGAGG AGCCCGAGGA GATGCGCGCC TCCCGCTTCC
11161 ACGCGGGGCG GGAGCTGCGG CGCGGCCTGG ACCGAAAGCG GGTGCTGAGG GACGAGGATT
11221 TCGAGGCGGA CGAGCTGACG GGGATCAGCC CCGCGCGCGC GCACGTGGCC GCGGCCAACC
11281 TGGTCACGGC GTACGAGCAG ACCGTGAAGG AGGAGAGCAA CTTCCAAAAA TCCTTCAACA
11341 ACCACGTGCG CACGCTGATC GCGCGCGAGG AGGTGACCCT GGGCCTGATG CACCTGTGGG
11401 ACCTGCTGGA GGCCATCGTG CAGAACCCCA CGAGCAAGCC GCTGACGGCG CAGCTGTTTC
11461 TGGTGGTGCA GCACAGTCGG GACAACGAGA CGTTCAGGGA GGCGCTGCTG AATATCACCG
11521 AGCCCGAGGG CCGCTGGCTC CTGGACCTGG TGAACATTCT GCAGAGCATC GTGGTGCAGG
11581 AGCGCGGGCT GCCGCTGTCC GAGAAGCTGG CGGCTATCAA CTTCTCGGTG CTGAGCCTGG
11641 GCAAGTACTA CGCTAGGAAG ATCTACAAGA CCCCGTACGT GCCCATAGAC AAGGAGGTGA
11701 AGATCGACGG GTTTTACATG CGCATGACCC TGAAAGTGCT GACCCTGAGC GACGATCTGG
11761 GGGTGTACCG CAACGACAGG ATGCACCGCG CGGTGAGCGC CAGCCGCCGG CGCGAGCTGA
11821 GCGACCAGGA GCTGATGCAC AGCCTGCAGC GGGCCCTGAC CGGGGCCGGG ACCGAGGGGG
11881 AGAGCTACTT TGACATGGGC GCGGACCTGC GCTGGCAGCC CAGCCGCCGG GCCTTGGAAG
11941 CTGCCGGCGG TTCCCCCTAC GTGGAGGAGG TGGACGATGA GGAGGAGGAG GGCGAGTACC
12001 TGGAAGACTG ATGGCGCGAC CGTATTTTTG CTAGATGCAG CAACAGCCAC CGCCTCCTGA
12061 TCCCGCGATG CGGGCGGCGC TGCAGAGCCA GCCGTCCGGC ATTAACTCCT CGGACGATTG
12121 GACCCAGGCC ATGCAACGCA TCATGGCGCT GACGACCCGC AATCCCGAAG CCTTTAGACA
12181 GCAGCCTCAG GCCAACCGGC TCTCGGCCAT CCTGGAGGCC GTGGTGCCCT CGCGCTCGAA
12241 CCCCACGCAC GAGAAGGTGC TGGCCATCGT GAACGCGCTG GTGGAGAACA AGGCCATCCG
12301 CGGCGACGAG GCCGGGCTGG TGTACAACGC GCTGCTGGAG CGCGTGGCCC GCTACAACAG
12361 CACCAACGTG CAGACGAACC TGGACCGCAT GGTGACCGAC GTGCGCGAGG CGGTGTCGCA
12421 GCGCGAGCGG TTCCACCGCG AGTCGAACCT GGGCTCCATG GTGGCGCTGA ACGCCTTCCT
12481 GAGCACGCAG CCCGCCAACG TGCCCCGGGG CCAGGAGGAC TACACCAACT TCATCAGCGC
12541 GCTGCGGCTG ATGGTGGCCG AGGTGCCCCA GAGCGAGGTG TACCAGTCGG GGCCGGACTA
12601 CTTCTTCCAG ACCAGTCGCC AGGGCTTGCA GACCGTGAAC CTGAGCCAGG CTTTCAAGAA
12661 CTTGCAGGGA CTGTGGGGCG TGCAGGCCCC GGTCGGGGAC CGCGCGACGG TGTCGAGCCT
12721 GCTGACGCCG AACTCGCGCC TGCTGCTGCT GCTGGTGGCG CCCTTCACGG ACAGCGGCAG
12781 CGTGAGCCGC GACTCGTACC TGGGCTACCT GCTTAACCTG TACCGCGAGG CCATCGGGCA
12841 GGCGCACGTG GACGAGCAGA CCTACCAGGA GATCACCCAC GTGAGCCGCG CGCTGGGCCA
12901 GGAGGACCCG GGCAACCTGG AGGCCACCCT GAACTTCCTG CTGACCAACC GGTCGCAGAA
12961 GATCCCGCCC CAGTACGCGC TGAGCACCGA GGAGGAGCGC ATCCTGCGCT ACGTGCAGCA
13021 GAGCGTGGGG CTGTTCCTGA TGCAGGAGGG GGCCACGCCC AGCGCCGCGC TCGACATGAC
13081 CGCGCGCAAC ATGGAGCCCA GCATGTACGC TCGCAACCGC CCGTTCATCA ATAAGCTGAT
13141 GGACTACTTG CATCGGGCGG CCGCCATGAA CTCGGACTAC TTTACCAACG CCATCTTGAA
13201 CCCGCACTGG CTCCCGCCGC CCGGGTTCTA CACGGGCGAG TACGACATGC CCGACCCCAA
13261 CGACGGGTTC CTGTGGGACG ACGTGGACAG CAGCGTGTTC TCGCCGCGCC CCGCCACCAC
13321 CGTGTGGAAG AAAGAGGGCG GGGACCGGCG GCCGTCCTCG GCGCTGTCCG GTCGCGCGGG
13381 TGCTGCCGCG GCGGTGCCTG AGGCCGCCAG CCCCTTCCCG AGCCTGCCCT TTTCGCTGAA
13441 CAGCGTGCGC AGCAGCGAGC TGGGTCGGCT GACGCGGCCG CGCCTGCTGG GCGAGGAGGA
13501 GTACCTGAAC GACTCCTTGT TGAGGCCCGA GCGCGAGAAG AACTTCCCCA ATAACGGGAT
13561 AGAGAGCCTG GTGGACAAGA TGAGCCGCTG GAAGACGTAC GCGCACGAGC ACAGGGACGA
13621 GCCCCGAGCT AGCAGCAGCG CAGGCACCCG TAGACGCCAG CGACACGACA GGCAGCGGGG
13681 TCTGGTGTGG GACGATGAGG ATTCCGCCGA CGACAGCAGC GTGTTGGACT TGGGTGGGAG
13741 TGGTGGTGGT AACCCGTTCG CTCACTTGCG CCCCCGTATC GGGCGCCTGA TGTAAGAATC
13801 TGAAAAAATA AAAAACGGTA CTCACCAAGG CCATGGCGAC CAGCGTGCGT TCTTCTCTGT
13861 TGTTTGTAGT AGTATGATGA GGCGCGTGTA CCCGGAGGGT CCTCCTCCCT CGTACGAGAG
13921 CGTGATGCAG CAGGCGGTGG CGGCGGCGAT GCAGCCCCCG CTGGAGGCGC CTTACGTGCC
13981 CCCGCGGTAC CTGGCGCCTA CGGAGGGGCG GAACAGCATT CGTTACTCGG AGCTGGCACC
14041 CTTGTACGAT ACCACCCGGT TGTACCTGGT GGACAACAAG TCGGCGGACA TCGCCTCGCT
14101 GAACTACCAG AACGACCACA GCAACTTCCT GACCACCGTG GTGCAGAACA ACGATTTCAC
14161 CCCCACGGAG GCCAGCACCC AGACCATCAA CTTTGACGAG CGCTCGCGGT GGGGCGGCCA
14281 GCTGAAAACC ATCATGCACA CCAACATGCC CAACGTGAAC GAGTTCATGT ACAGCAACAA
14281 GTTCAAGGCG CGGGTGATGG TCTCGCGCAA GACCCCCAAT GGGGTCGCGG TGGATGAGAA
```

Fig. 8D

SEQ ID No: 4


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14341 TTATGATGGT AGTCAGGACG AGCTGACTTA CGAGTGGGTG GAGTTTGAGC TGCCCGAGGG
14401 CAACTTCTCG GTGACCATGA CCATCGATCT GATGAACAAC GCCATCATCG ACAACTACTT
14461 GGCGGTGGGG CGTCAGAACG GGGTGCTGGA GAGCGACATC GGCGTGAAGT TCGACACGCG
14521 CAACTTCCGG CTGGGCTGGG ACCCCGTGAC CGAGCTGGTG ATGCCGGGCG TGTACACCAA
14581 CGAGGCCTTC CACCCCGACA TCGTCCTGCT GCCCGGCTGC GGCGTGGACT TCACCGAGAG
14641 CCGCCTCAGC AACCTGCTGG GCATCCGCAA GCGGCAGCCC TTCCAGGAGG GCTTCCAGAT
14701 CCTGTACGAG GACCTGGAGG GGGGCAACAT CCCCGCGCTC TTGGATGTCG AAGCCTATGA
14761 GAAAAGCAAG GAGGAGGCCG CCGCAGCGGC GACCGCAGCC GTGGCCACCG CCTCTACCGA
14821 GGTGCGGGGC GATAATTTTG CTAGCGCCGC GGCAGTGGCC GAGGCGGCTG AAACCGAAAG
14881 TAAGATAGTC ATCCAGCCGG TGGAGAAGGA CAGCAAGGAC AGGAGCTACA ACGTGCTCGC
14941 GGACAAGAAA AACACCGCCT ACCGCAGCTG GTACCTGGCC TACAACTACG GCGACCCCGA
15001 GAAGGGCGTG CGCTCCTGGA CGCTGCTCAC CACCTCGGAC GTCACCTGCG GCGTGGAGCA
15061 AGTCTACTGG TCGCTGCCCG ACATGATGCA AGACCCGGTC ACCTTCCGCT CCACGCGTCA
15121 AGTTAGCAAC TACCCGGTGG TGGGCGCCGA GCTCCTGCCC GTCTACTCCA AGAGCTTCTT
15181 CAACGAGCAG GCCGTCTACT CGCAGCAGCT GCGCGCCTTC ACCTCGCTCA CGCACGTCTT
15241 CAACCGCTTC CCCGAGAACC AGATCCTCGT CCGCCCGCCC GCGCCCACCA TTACCACCGT
15301 CAGTGAAAAC GTTCCTGCTC TCACAGATCA CGGGACCCTG CCGCTGCGCA GCAGTATCCG
15361 GGGAGTCCAG CGCGTGACCG TCACTGACGC CAGACGCCGC ACCTGCCCCT ACGTCTACAA
15421 GGCCCTGGGC GTAGTCGCGC CGCGCGTCCT CTCGAGCCGC ACCTTCTAAA AAATGTCCAT
15481 TCTCATCTCG CCCAGTAATA ACACCGGTTG GGGCCTGCGC GCGCCCAGCA AGATGTACGG
15541 AGGCGCTCGC CAACGCTCCA CGCAACACCC CGTGCGCGTG CGCGGGCACT TCCGCGCTCC
15601 CTGGGGCGCC CTCAAGGGCC GCGTGCGCTC GCGCACCACC GTCGACGACG TGATCGACCA
15661 GGTGGTGGCC GACGCGCGCA ACTACACGCC CGCCGCCGCG CCCGCCTCCA CCGTGGACGC
15721 CGTCATCGAC AGCGTGGTGG CCGATGCGCG CCGGTACGCC CGCGCCAAGA GCCGGCGGCG
15781 GCGCATCGCC CGGCGGCACC GGAGCACCCC CGCCATGCGC GCGGCGCGAG CCTTGCTGCG
15841 CAGGGCCAGG CGCACGGGAC GCAGGGCCAT GCTCAGGGCG GCCAGACGCG CGGCCTCCGG
15901 CAGCAGCAGC GCCGGCAGGA CCCGCAGACG CGCGGCCACG GCGGCGGCGG CGGCCATCGC
15961 CAGCATGTCC CGCCCGCGGC GCGGCAACGT GTACTGGGTG CGCGACGCCG CCACCGGTGT
16021 GCGCGTGCCC GTGCGCACCC GCCCCCCTCG CACTTGAAGA TGCTGACTTC GCGATGTTGA
16081 TGTGTCCCAG CGGCGAGGAG GATGTCCAAG CGCAAATACA AGGAAGAGAT GCTCCAGGTC
16141 ATCGCGCCTG AGATCTACGG CCCCGCGGTG AAGGAGGAAA GAAAGCCCCG CAAACTGAAG
16201 CGGGTCAAAA AGGACAAAAA GGAGGAGGAA GATGTGGACG GACTGGTGGA GTTTGTGCGC
16261 GAGTTCGCCC CCCGGCGGCG CGTGCAGTGG CGCGGGCGGA AAGTGAAACC GGTGCTGCGG
16321 CCCGGCACCA CGGTGGTCTT CACGCCCGGC GAGCGTTCCG GCTCCGCCTC CAAGCGCTCC
16381 TACGACGAGG TGTACGGGGA CGAGGACATC CTCGAGCAGG CGGTCGAGCG TCTGGGCGAG
16441 TTTGCTTACG GCAAGCGCAG CCGCCCCGCG CCCTTGAAAG AGGAGGCGGT GTCCATCCCG
16501 CTGGACCACG GCAACCCCAC GCCGAGCCTG AAGCCGGTGA CCCTGCAGCA GGTGCTGCCG
16561 AGCGCGGCGC CGCGCCGGGG CTTCAAGCGC GAGGGCGGCG AGGATCTGTA CCCGACCATG
16621 CAGCTGATGG TGCCCAAGCG CCAGAAGCTG GAGGACGTGC TGGAGCACAT GAAGGTGGAC
16681 CCCGAGGTGC AGCCCGAGGT CAAGGTGCGG CCCATCAAGC AGGTGGCCCC GGGCCTGGGC
16741 GTGCAGACCG TGGACATCAA GATCCCCACG GAGCCCATGG AAACGCAGAC CGAGCCCGTG
16801 AAGCCCAGCA CCAGCACCAT GGAGGTGCAG ACGGATCCCT GGATGCCGGC GCCGGCTTCC
16861 ACCACTCGCC GAAGACGCAA GTACGGCGCG GCCAGCCTGC TGATGCCCAA CTACGCGCTG
16921 CATCCTTCCA TCATCCCCAC GCCGGGCTAC CGCGGCACGC GCTTCTACCG CGGCTACACC
16981 AGCAGCCGCC GCAAGACCAC CACCCGCCGC CGCCGTCGTC GCACCCGCCG CAGCAGCACC
17041 GCGACTTCCG CCGCCGCCCT GGTGCGGAGA GTGTACCGCA GCGGGCGCGA GCCTCTGACC
17101 CTGCCGCGCG CGCGCTACCA CCCGAGCATC GCCATTTAAC TCTGCCGTCG CCTCCTACTT
17161 GCAGATATGG CCCTCACATG CCGCCTCCGC GTCCCCATTA CGGGCTACCG AGGAAGAAAG
17221 CCGCGCCGTA GAAGGCTGAC GGGGAACGGG CTGCGTCGCC ATCACCACCG GCGGCGGCGC
17281 GCCATCAGCA AGCGGTTGGG GGGAGGCTTC CTGCCCGCGC TGATCCCCAT CATCGCCGCG
17341 GCGATCGGGG CGATCCCCGG CATAGCTTCC GTGGCGGTGC AGGCCTCTCA GCGCCACTGA
17401 GACACAGCTT GGAAAATTTG TAATAAAAAA ATGGACTGAC GCTCCTGGTC CTGTGATGTG
17461 TGTTTTTAGA TGGAAGACAT CAATTTTTCG TCCCTGGCAC CGCGACACGG CACGCGGCCG
17521 TTTATGGGCA CCTGGAGCGA CATCGGCAAC AGCCAACTGA ACGGGGGCGC CTTCAATTGG
17581 AGCAGTCTCT GGAGCGGGCT TAAGAATTTC GGGTCCACGC TCAAAACCTA TGGCAACAAG
17641 GCGTGGAACA GCAGCACAGG GCAGGCGCTG AGGGAAAAGC TGAAAGAGCA GAACTTCCAG
17701 CAGAAGGTGG TCGATGGCCT GGCCTCGGGC ATCAACGGGG TGGTGGACCT GGCCAACCAG
17761 GCCGTGCAGA AACAGATCAA CAGCCGCCTG GACGCGGTCC CGCCCGCGGG GTCCGTGGAG
17821 ATGCCCCAGG TGGAGGAGGA GCTGCCTCCC CTGGACAAGC GCGGCGACAA GCGACCGCGT
17881 CCCGACGCGG AGGAGACGCT GCTGACGCAC ACGGACGAGC CGCCCCCGTA CGAGGAGGCG
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Fig. 8E

SEQ ID No: 4


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17941 GTGAAACTGG GTCTGCCCAC CACGCGGCCC GTGGCGCCTC TGGCCACCGG GGTGCTGAAA
18001 CCCAGCAGCA GCAGCCAGCC CGCGACCCTG GACTTGCCTC CGCCTGCTTC CCGCCCCTCC
18061 ACAGTGGCTA AGCCCCTGCC GCCGGTGGCC GTCGCGTCGC GCGCCCCCCG AGGCCGCCCC
18121 CAGGCGAACT GGCAGAGCAC TCTGAACAGC ATCGTGGGTC TGGGAGTGCA GAGTGTGAAG
18181 CGCCGCCGCT GCTATTAAAA GACACTGTAG CGCTTAACTT GCTTGTCTGT GTGTATATGT
18241 ATGTCCGCCG ACCAGAAGGA GGAAGAGGCG CGTCGCCGAG TTGCAAGATG GCCACCCCAT
18301 CGATGCTGCC CCAGTGGGCG TACATGCACA TCGCCGGACA GGACGCTTCG GAGTACCTGA
18361 GTCCGGGTCT GGTGCAGTTC GCCCGCGCCA CAGACACCTA CTTCAGTCTG GGGAACAAGT
18421 TTAGGAACCC CACGGTGGCG CCCACGCACG ATGTGACCAC CGACCGCAGC CAGCGGCTGA
18481 CGCTGCGCTT CGTGCCCGTG GACCGCGAGG ACAACACCTA CTCGTACAAA GTGCGCTACA
18541 CGCTGGCCGT GGGCGACAAC CGCGTGCTGG ACATGGCCAG CACCTACTTT GACATCCGCG
18601 GCGTGCTGGA TCGGGGGCCC AGCTTCAAAC CCTACTCCGG CACCGCCTAC AACAGCCTGG
18661 CTCCCAAGGG AGCGCCCAAC ACTTGCCAGT GGACATATAA AGCTGGTGAT ACTGATACAG
18721 AAAAAACCTA TACATATGGA AATGCACCTG TGCAAGGCAT TAGCATTACA AAGGATGGTA
18781 TTCAACTTGG AACTGACAGC GATGGTCAGG CAATCTATGC AGACGAAACT TATCAACCAG
18841 AGCCTCAAGT GGGTGATGCT GAATGGCATG ACATCACTGG TACTGATGAA AAATATGGAG
18901 GCAGAGCTCT TAAGCCTGAC ACCAAAATGA AGCCTTGCTA TGGTTCTTTT GCCAAGCCTA
18961 CCAATAAAGA AGGAGGCCAG GCAAATGTGA AAACCGAAAC AGGCGGTACC AAAGAATATG
19021 ACATTGACAT GGCATTCTTC GATAATCGAA GTGCAGCTGC CGCCGGCCTA GCCCCAGAAA
19081 TTGTTTTGTA TACTGAGAAT GTGGATCTGG AAACTCCAGA TACCCATATT GTATACAAGG
19141 CAGGTACAGA TGACAGTAGC TCTTCTATCA ATTTGGGTCA GCAGTCCATG CCCAACAGAC
19201 CCAACTACAT TGGCTTCAGA GACAACTTTA TCGGTCTGAT GTACTACAAC AGCACTGGCA
19261 ATATGGGTGT ACTGGCTGGA CAGGCCTCCC AGCTGAATGC TGTGGTGGAC TTGCAGGACA
19321 GAAACACCGA ACTGTCCTAC CAGCTCTTGC TTGACTCTCT GGGTGACAGA ACCAGGTATT
19381 TCAGTATGTG GAATCAGGCG GTGGACAGTT ATGACCCCGA TGTGCGCATT ATTGAAAATC
19441 ACGGTGTGGA GGATGAACTT CCTAACTATT GCTTCCCCCT GGATGCTGTG GGTAGAACTG
19501 ATACTTACCA GGGAATTAAG GCCAATGGTG ATAATCAAAC CACCTGGACC AAAGATGATA
19561 CTGTTAATGA TGCTAATGAA TTGGGCAAGG GCAATCCTTT CGCCATGGAG ATCAACATCC
19621 AGGCCAACCT GTGGCGGAAC TTCCTCTACG CGAACGTGGC GCTGTACCTG CCCGACTCCT
19681 ACAAGTACAC GCCGGCCAAC ATCACGCTGC CCACCAACAC CAACACCTAC GATTACATGA
19741 ACGGCCGCGT GGTGGCGCCC TCGCTGGTGG ACGCCTACAT CAACATCGGG GCGCGCTGGT
19801 CGCTGGACCC CATGGACAAC GTCAACCCCT TCAACCACCA CCGCAACGCG GGCCTGCGAT
19861 ACCGCTCCAT GCTCCTGGGC AACGGGCGCT ACGTGCCCTT CCACATCCAG GTGCCCCAAA
19921 AGTTTTTCGC CATCAAGAGC CTCCTGCTCC TGCCCGGGTC CTACACCTAC GAGTGGAACT
19981 TCCGCAAGGA CGTCAACATG ATCCTGCAGA GCTCCCTCGG CAACGACCTG CGCACGGACG
20041 GGGCCTCCAT CGCCTTCACC AGCATCAACC TCTACGCCAC CTTCTTCCCC ATGGCGCACA
20101 ACACCGCCTC CACGCTCGAG GCCATGCTGC GCAACGACAC CAACGACCAG TCCTTCAACG
20161 ACTACCTCTC GGCGGCCAAC ATGCTCTACC CCATCCCGGC CAACGCCACC AACGTGCCCA
20221 TCTCCATCCC CTCGCGCAAC TGGGCCGCCT TCCGCGGCTG GTCCTTCACG CGCCTCAAGA
20281 CCCGCGAGAC GCCCTCGCTC GGCTCCGGGT TCGACCCCTA CTTCGTCTAC TCGGGCTCCA
20341 TCCCCTACCT CGACGGCACC TTCTACCTCA ACCACACCTT CAAGAAGGTC TCCATCACCT
20401 TCGACTCCTC CGTCAGCTGG CCCGGCAACG ACCGCCTCCT GACGCCCAAC GAGTTCGAAA
20461 TCAAGCGCAC CGTCGACGGA GAGGGGTACA ACGTGGCCCA GTGCAACATG ACCAAGGACT
20521 GGTTCCTGGT CCAGATGCTG GCCCACTACA ACATCGGCTA CCAGGGCTTC TACGTGCCCG
20581 AGGGCTACAA GGACCGCATG TACTCCTTCT TCCGCAACTT CCAGCCCATG AGCCGCCAGG
20641 TCGTGGACGA GGTCAACTAC AAGGACTACC AGGCCGTCAC CCTGGCCTAC CAGCACAACA
20701 ACTCGGGCTT CGTCGGCTAC CTCGCGCCCA CCATGCGCCA GGGCCAGCCC TACCCCGCCA
20761 ACTACCCCTA CCCGCTCATC GGCAAGAGCG CCGTCGCCAG CGTCACCCAG AAAAAGTTCC
20821 TCTGCGACCG GGTCATGTGG CGCATCCCCT TCTCCAGCAA CTTCATGTCC ATGGGCGCGC
20881 TCACCGACCT CGGCCAGAAC ATGCTCTACG CCAACTCCGC CCACGCGCTA GACATGAATT
20941 TCGAAGTCGA CCCCATGGAT GAGTCCACCC TTCTCTATGT TGTCTTCGAA GTCTTCGACG
21001 TCGTCCGAGT GCACCAGCCC CACCGCGGCG TCATCGAGGC CGTCTACCTG CGCACGCCCT
21061 TCTCGGCCGG CAACGCCACC ACCTAAGCCT CTTGCTTCTT GCAAGATGAC GGCCTGCGCG
21121 GGCTCCGGCG AGCAGGAGCT CAGGGCCATC CTCCGCGACC TGGGCTGCGG GCCCTGCTTC
21181 CTGGGCACCT TCGACAAGCG CTTCCCGGGA TTCATGGCCC CGCACAAGCT GGCCTGCGCC
21241 ATCGTCAACA CGGCCGGCCG CGAGACCGGG GGCGAGCACT GGCTGGCCTT CGCCTGGAAC
21301 CCGCGCTCCC ACACCTGCTA CCTCTTCGAC CCCTTCGGGT TCTCGGACGA GCGCCTCAAG
21361 CAGATCTACC AGTTCGAGTA CGAGGGCCTG CTGCGTCGCA GCGCCCTGGC CACCGAGGAC
21421 CGCTGCGTCA CCCTGGAAAA GTCCACCCAG ACCGTGCAGG GTCCGCGCTC GGCCGCCTGC
21481 GGGCTCTTCT GCTGCATGTT CCTGCACGCC TTCGTGCACT GGCCCGACCG CCCCATGGAC
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Fig. 8F

SEQ ID No: 4


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21541 AAGAACCCCA CCATGAACTT GCTGACGGGG GTGCCCAACG GCATGCTCCA GTCGCCCCAG
21601 GTGGAACCCA CCCTGCGCCG CAACCAGGAG GCGCTCTACC GCTTCCTCAA CGCCCACTCC
21661 GCCTACTTTC GCTCCCACCG CGCGCGCATC GAGAAGGCCA CCGCCTTCGA CCGCATGAAT
21721 CAAGACATGT AATCCGGTGT GTGTATGTGA ATGCTTTATT CATCATAATA AACAGCACAT
21781 GTTTATGCCA CCTTCTCTGA GGCTCTGACT TTATTTAGAA ATCGAAGGGG TTCTGCCGGC
21841 TCTCGGCATG GCCCGCGGGC AGGGATACGT TGCGGAACTG GTACTTGGGC AGCCACTTGA
21901 ACTCGGGGAT CAGCAGCTTC GGCACGGGGA GGTCGGGGAA CGAGTCGCTC CACAGCTTGC
21961 GCGTGAGTTG CAGGGCGCCC AGCAGGTCGG GCGCGGAGAT CTTGAAATCG CAGTTGGGAC
22021 CCGCGTTCTG CGCGCGAGAG TTACGGTACA CGGGGTTGCA GCACTGGAAC ACCATCAGGG
22081 CCGGGTGCTT CACGCTCGCC AGCACCGTCG CGTCGGTGAT GCCCTCCACG TCCAGATCCT
22141 CGGCGTTGGC CATCCCGAAG GGGGTCATCT TGCAGGTCTG CCGCCCCATG CTGGGCACGC
22201 AGCCGGGCTT GTGGTTGCAA TCGCAGTGCA GGGGGATCAG CATCATCTGG GCCTGCTCGG
22261 AGCTCATGCC CGGGTACATG GCCTTCATGA AAGCCTCCAG CTGGCGGAAG GCCTGCTGCG
22321 CCTTGCCGCC CTCGGTGAAG AAGACCCCGC AGGACTTGCT AGAGAACTGG TTGGTGGCGC
22381 AGCCAGCGTC GTGCACGCAG CAGCGCGCGT CGTTGTTGGC CAGCTGCACC ACGCTGCGCC
22441 CCCAGCGGTT CTGGGTGATC TTGGCCCGGT CGGGGTTCTC CTTCAGCGCG CGCTGCCCGT
22501 TCTCGCTCGC CACATCCATC TCGATCGTGT GCTCCTTCTG GATCATCACG GTCCCGTGCA
22561 GGCACCGCAG CTTGCCCTCG GCCTCGGTGC ACCCGTGCAG CCACAGCGCG CAGCCGGTGC
22621 TCTCCCAGTT CTTGTGGGCG ATCTGGGAGT GCGAGTGCAC GAAGCCCTGC AGGAAGCGGC
22681 CCATCATCGT GGTCAGGGTC TTGTTGCTGG TGAAGGTCAG CGGAATGCCG CGGTGCTCCT
22741 CGTTCACATA CAGGTGGCAG ATACGGCGGT ACACCTCGCC CTGCTCGGGC ATCAGCTGGA
22801 AGGCGGACTT CAGGTCGCTC TCCACGCGGT ACCGGTCCAT CAGCAGCGTC ATCACTTCCA
22861 TGCCCTTCTC CCAGGCCGAA ACGATCGGCA GGCTCAGGGG GTTCTTCACC GTTGTCATCT
22921 TAGTCGCCGC CGCCGAAGTC AGGGGGTCGT TCTCGTCCAG GGTCTCAAAC ACTCGCTTGC
22981 CGTCCTTCTC GGTGATGCGC ACGGGGGGAA AGCTGAAGCC CACGGCCGCC AGCTCCTCCT
23041 CGGCCTGCCT TTCGTCCTCG CTGTCCTGGC TGATGTCTTG CAAAGGCACA TGCTTGGTCT
23101 TGCGGGGTTT CTTTTTGGGC GGCAGAGGCG GCGGCGGAGA CGTGCTGGGC GAGCGCGAGT
23161 TCTCGCTCAC CACGACTATT TCTTCTCCTT GGCCGTCGTC CGAGACCACG CGGCGGTAGG
23221 CATGCCTCTT CTGGGGCAGA GGCGGAGGCG ACGGGCTCTC GCGGTTCGGC GGGCGGCTGG
23281 CAGAGCCCCT TCCGCGTTCG GGGGTGCGCT CCTGGCGGCG CTGCTCTGAC TGACTTCCTC
23341 CGCGGCCGGC CATTGTGTTC TCCTAGGGAG CAAGCATGGA GACTCAGCCA TCGTCGCCAA
23401 CATCGCCATC TGCCCCCGCC GCCGCCGACG AGAACCAGCA GCAGCAGAAT GAAAGCTTAA
23461 CCGCCCCGCC GCCCAGCCCC ACCTCCGACG CCGCAGCCCC AGACATGCAA GAGATGGAGG
23521 AATCCATCGA GATTGACCTG GGCTACGTGA CGCCCGCGGA GCACGAGGAG GAGCTGGCAG
23581 CGCGCTTTTC AGCCCCGGAA GAGAACCACC AAGAGCAGCC AGAGCAGGAA GCAGAGAGCG
23641 AGCAGAACCA GGCTGGGCTC GAGCATGGCG ACTACCTGAG CGGGGCAGAG GACGTGCTCA
23701 TCAAGCATCT GGCCCGCCAA TGCATCATCG TCAAGGACGC GCTGCTCGAC CGCGCCGAGG
23761 TGCCCCTCAG CGTGGCGGAG CTCAGCCGCG CCTACGAGCG CAACCTCTTC TCGCCGCGCG
23821 TGCCCCCCAA GCGCCAGCCC AACGGCACCT GCGAGCCCAA CCCGCGCCTC AACTTCTACC
23881 CGGTCTTCGC GGTGCCCGAG GCCCTGGCCA CCTACCACCT CTTTTTCAAG AACCAAAGGA
23941 TCCCCGTCTC CTGCCGCGCC AACCGCACCC GCGCCGACGC CCTGCTCAAC CTGGGCCCCG
24001 GCGCCCGCCT ACCTGATATC GCCTCCTTGG AAGAGGTTCC CAAGATCTTC GAGGGTCTGG
24061 GCAGCGACGA GACTCGGGCC GCGAACGCTC TGCAAGGAAG CGGAGAGGAG CATGAGCACC
24121 ACAGCGCCCT GGTGGAGTTG GAAGGCGACA ACGCGCGCCT GGCGGTCCTC AAGCGCACGG
24181 TCGAGCTGAC CCACTTCGCC TACCCGGCGC TCAACCTGCC CCCCAAGGTC ATGAGCGCCG
24241 TCATGGACCA GGTGCTCATC AAGCGCGCCT CGCCCCTCTC GGAGGAGGAG ATGCAGGACC
24301 CCGAGAGCTC GGACGAGGGC AAGCCCGTGG TCAGCGACGA GCAGCTGGCG CGCTGGCTGG
24361 GAGCGAGTAG CACCCCCCAG AGCCTGGAAG AGCGGCGCAA GCTCATGATG GCCGTGGTCC
24421 TGGTGACCGT GGAGCTGGAG TGTCTGCGCC GCTTCTTCGC CGACGCGGAG ACCCTGCGCA
24481 AGGTCGAGGA GAACCTGCAC TACCTCTTCA GACACGGGTT CGTGCGCCAG GCCTGCAAGA
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24601 TGGGGCAGAA CGTGCTGCAC ACCACCCTGC GCGGGGAGGC CCGCCGCGAC TACATCCGCG
24661 ACTGCGTCTA CCTGTACCTC TGCCACACCT GGCAGACGGG CATGGGCGTG TGGCAGCAGT
24721 GCCTGGAGGA GCAGAACCTG AAAGAGCTCT GCAAGCTCCT GCAGAAGAAC CTCAAGGCCC
24781 TGTGGACCGG GTTCGACGAG CGCACCACCG CCGCGGACCT GGCCGACCTC ATCTTCCCCG
24841 AGCGCCTGCG GCTGACGCTG CGCAACGGGC TGCCCGACTT TATGAGCCAA AGCATGTTGC
24901 AAAACTTTCG CTCTTTCATC CTCGAACGCT CCGGGATCCT GCCCGCCACC TGCTCCGCGC
24961 TGCCCTCGGA CTTCGTGCCG CTGACCTTCC GCGAGTGCCC CCCGCCGCTC TGGAGCCACT
25021 GCTACCTGCT GCGCCTGGCC AACTACCTGG CCTACCACTC GGACGTGATC GAGGACGTCA
25081 GCGGCGAGGG CCTGCTCGAG TGCCACTGCC GCTGCAACCT CTGCACGCCG CACCGCTCCC
```

Fig. 8G

SEQ ID No: 4


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25141 TGGCCTGCAA CCCCCAGCTG CTGAGCGAGA CCCAGATCAT CGGCACCTTC GAGTTGCAAG
25201 GCCCCGGCGA GGGCAAGGGG GGTCTGAAAC TCACCCCGGG GCTGTGGACC TCGGCCTACT
25261 TGCGCAAGTT CGTGCCCGAG GACTACCATC CCTTCGAGAT CAGGTTCTAC GAGGACCAAT
25321 CCCAGCCGCC CAAGGCCGAG CTGTCGGCCT GCGTCATCAC CCAGGGGGCC ATCCTGGCCC
25381 AATTGCAAGC CATCCAGAAA TCCCGCCAAG AATTTCTGCT GAAAAAGGGC CACGGGGTCT
25441 ACTTGGACCC CCAGACCGGA GAGGAGCTCA ACCCCAGCTT CCCCCAGGAT GCCCCGAGGA
25501 AGCAGCAAGA AGCTGAAAGT GGAGCTGCCG CCGCCGCCGG AGGATTTGGA GGAAGACTGG
25561 GAGAGCAGTC AGGCAGAGGA GGAGGAGATG GAAGACTGGG ACAGCACTCA GGCAGAGGAG
25621 GACAGCCTGC AAGACAGTCT GGAGGAGGAA GACGAGGTGG AGGAGGCAGA GGAAGAAGCA
25681 GCCGCCGCCA GACCGTCGTC CTCGGCGGAG GAGGAGAAAG CAAGCAGCAC GGATACCATC
25741 TCCGCTCCGG GTCGGGGTCG CGGCGGCCGG GCCCACAGTA GATGGGACGA GACCGGGCGC
25801 TTCCCGAACC CCACCACCCA GACCGGTAAG AAGGAGCGGC AGGGATACAA GTCCTGGCGG
25861 GGGCACAAAA ACGCCATCGT CTCCTGCTTG CAAGCCTGCG GGGGCAACAT CTCCTTCACC
25921 CGGCGCTACC TGCTCTTCCA CCGCGGGGTG AACTTCCCCC GCAACATCTT GCATTACTAC
25981 CGTCACCTCC ACAGCCCCTA CTACTGTTTC CAAGAAGAGG CAGAAACCCA GCAGCAGCAG
26041 CAGCAGCAGA AAACCAGCGG CAGCAGCTAG AAAATCCACA GCGGCGGCAG GTGGACTGAG
26101 GATCGCGGCG AACGAGCCGG CGCAGACCCG GGAGCTGAGG AACCGGATCT TTCCCACCCT
26161 CTATGCCATC TTCCAGCAGA GTCGGGGGCA AGAGCAGGAA CTGAAAGTCA AGAACCGTTC
26221 TCTGCGCTCG CTCACCCGCA GTTGTCTGTA TCACAAGAGC GAAGACCAAC TTCAGCGCAC
26281 TCTCGAGGAC GCCGAGGCTC TCTTCAACAA GTACTGCGCG CTCACTCTTA AAGAGTAGCC
26341 CGCGCCCGCC CACACACGGA AAAAGGCGGG AATTACGTCA CCACCTGCGC CCTTCGCCCG
26401 ACCATCATCA TGAGCAAAGA GATTCCCACG CCTTACATGT GGAGCTACCA GCCCCAGATG
26461 GGCCTGGCCG CCGGCGCCGC CCAGGACTAC TCCACCCGCA TGAACTGGCT CAGTGCCGGG
26521 CCCGCGATGA TCTCACGGGT GAATGACATC CGCGCCCACC GAAACCAGAT ACTCCTAGAA
26581 CAGTCAGCGA TCACCGCCAC GCCCCGCCAT CACCTTAATC CGCGTAATTG GCCCGCCGCC
26641 CTGGTGTACC AGGAAATTCC CCAGCCCACG ACCGTACTAC TTCCGCGAGA CGCCCAGGCC
26701 GAAGTCCAGC TGACTAACTC AGGTGTCCAG CTGGCCGGCG GCGCCGCCCT GTGTCGTCAC
26761 CGCCCCGCTC AGGGTATAAA GCGGCTGGTG ATCCGAGGCA GAGGCACACA GCTCAACGAC
26821 GAGGTGGTGA GCTCTTCGCT GGGTCTGCGA CCTGACGGAG TCTTCCAACT CGCCGGATCG
26881 GGGAGATCTT CCTTCACGCC TCGTCAGGCC GTCCTGACTT TGGAGAGTTC GTCCTCGCAG
26941 CCCCGCTCGG GTGGCATCGG CACTCTCCAG TTCGTGGAGG AGTTCACTCC CTCGGTCTAC
27001 TTCAACCCCT TCTCCGGCTC CCCCGGCCAC TACCCGGACG AGTTCATCCC GAACTTCGAC
27061 GCCATCAGCG AGTCGGTGGA CGGCTACGAT TGAATGTCCC ATGGTGGCGC GGCTGACCTA
27121 GCTCGGCTTC GACACCTGGA CCACTGCCGC CGCTTCCGCT GCTTCGCTCG GGATCTCGCC
27181 GAGTTTGCCT ACTTTGAGCT GCCCGAGGAG CACCCTCAGG GCCCGGCCCA CGGAGTGCGG
27241 ATCGTCGTCG AAGGGGGTCT CGACTCCCAC CTGCTTCGGA TCTTCAGCCA GCGTCCGATC
27301 CTGGCCGAGC GCGAGCAAGG ACAGACCCTT CTGACCCTGT ACTGCATCTG CAACCACCCC
27361 GGCCTGCATG AAAGTCTTTG TTGTCTGCTG TGTACTGAGT ATAATAAAAG CTGAGATCAG
27421 CGACTACTCC GGACTTCCGT GTGTTCCTGC TATCAACCAG TCCCTGTTCT TCACCGGGAA
27481 CGAGACCGAG CTCCAGCTCC AGTGTAAGCC CCACAAGAAG TACCTCACCT GGCTGTTCCA
27541 GGGCTCTCCG ATCGCCGTTG TCAACCACTG CGACAACGAC GGAGTCCTGC TGAGCGGCCC
27601 TGCCAACCTT ACTTTTTCCA CCCGCAGAAG CAAGCTCCAG CTCTTCCAAC CCTTCCTCCC
27661 CGGGACCTAT CAGTGCGTCT CGGGACCCTG CCATCACACC TTCCACCTGA TCCCGAATAC
27721 CACAGCGTCG CTCCCCGCTA CTAACAACCA AACTACCCAC CAACGCCACC GTCGCGACCT
27781 TTCCTCTGGG TCTAATACCA CTACCGGAGG TGAGCTCCGA GGTCGACCAA CCTCTGGGAT
27841 TTACTACGGC CCCTGGGAGG TGGTAGGGTT AATAGCGCTA GGCCTAGTTG CGGGTGGGCT
27901 TTTGGCTCTC TGCTACCTAT ACCTCCCTTG CTGTTCGTAC TTAGTGGTGC TGTGTTGCTG
27961 GTTTAAGAAA TGGGGAAGAT CACCCTAGTG AGCTGCGGTG TGCTGGTGGC GGTGGTGCTT
28021 TCGATTGTGG GACTGGGCGG CGCGGCTGTA GTGAAGGAGA AGGCCGATCC CTGCTTGCAT
28081 TTCAATCCCG ACAAATGCCA GCTGAGTTTT CAGCCCGATG GCAATCGGTG CGCGGTGCTG
28141 ATCAAGTGCG GATGGGAATG CGAGAACGTG AGAATCGAGT ACAATAACAA GACTCGGAAC
28201 AATACTCTCG CGTCCGTGTG GCAGCCCGGG GACCCCGAGT GGTACACCGT CTCTGTCCCC
28261 GGTGCTGACG GCTCCCCGCG CACCGTGAAT AATACTTTCA TTTTTGCGCA CATGTGCGAC
28321 ACGGTCATGT GGATGAGCAA GCAGTACGAT ATGTGGCCCC CCACGAAGGA GAACATCGTG
28381 GTCTTCTCCA TCGCTTACAG CGTGTGCACG GCGCTAATCA CCGCTATCGT GTGCCTGAGC
28441 ATTCACATGC TCATCGCTAT TCGCCCCAGA AATAATGCCG AAAAAGAAAA ACAGCCATAA
28501 CACGTTTTTT CACACACCTT TTTCAGACCA TGGCCTCTGT TAAATTTTTG CTTTTATTTG
28561 CCAGTCTCAT TGCCGTCATT CATGGAATGA GTAATGAGAA AATTACTATT TACACTGGCA
28621 CTAATCACAC ATTGAAAGGT CCAGAAAAAG CCACAGAAGT TTCATGGTAT TGTTATTTTA
28681 ATGAATCAGA TGTATCTACT GAACTCTGTG GAAACAATAA CAAAAAAAAT GAGAGCATTA
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Fig. 8H

SEQ ID No: 4

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28741 CTCTCATCAA GTTTCAATGT GGATCTGACT TAACCCTAAT TAACATCACT AGAGACTATG
28801 TAGGTATGTA TTATGGAACT ACAGCAGGCA TTTCGGACAT GGAATTTTAT CAAGTTTCTG
28861 TGTCTGAACC CACCACGCCT AGAATGACCA CAACCACAAA AACTACACCT GTTACCACTA
28921 TACAGCTCAC TACCAATGGC TTTCTTGCCA TGCTTCAAGT GGCTGAAAAT AGCACCAGCA
28981 TTCAACCCAC CCCACCCAGT GAGGAAATTC CCAGATCCAT GATTGGCATT ATTGTTGCTG
29041 TAGTGGTGTG CATGTTGATC ATCGCCTTGT GCATGGTGTA CTATGCCTTC TGCTACAGAA
29101 AGCACAGACT GAACGACAAG CTGGAACACT TACTAAGTGT TGAATTTTAA TTTTTTAGAA
29161 CCATGAAGAT CCTAGGCCTT TTAGTTTTTT CTATCATTAC CTCTGCTCTA TGCAATTCTG
29221 ACAATGAGGA CGTTACTGTC GTTGTCGGAT CAAATTATAC ACTAAAAGGT CCAGCAAAAG
29281 GTATGCTTTC GTGGTATTGT TGGTTCGGAA CTGACGAGCA ACAGACAGAA CTTTGCAATG
29341 CTCAAAAAGG CAAAACCTCA AATTCTAAAA TCTCTAATTA TCAATGCAAT GGCACTGACT
29401 TAGTATTGCT CAATGTCACG AAAGCATATG CTGGCAGTTA CACCTGCCCT GGAGATGATG
29461 CCGACAATAT GATTTTTTAC AAAGTGGAAG TGGTTGATCC CACTACTCCA CCGCCCACCA
29521 CCACAACTAC TCATACCACA CACACAGAAC AAACACCAGA GGCAGCAGAA GCAGAGTTGG
29581 CCTTCCAGGT TCACGGAGAT TCCTTTGCTG TCAATACCCC TACACCCGAT CAGCGGTGTC
29641 CGGGGCTGCT CGTCAGCGGC ATTGTCGGTG TGCTTTCGGG ATTAGCAGTC ATAATCATCT
29701 GCATGTTCAT TTTTGCTTGC TGCTATAGAA GGCTTTACCG ACAAAAATCA GACCCACTGC
29761 TGAACCTCTA TGTTTAATTT TTTCCAGAGC CATGAAGGCA GTTAGCGCTC TAGTTTTTTG
29821 TTCTTTGATT GGCATTGTTT TTAGTGCTGG GTTTTTGAAA AATCTTACCA TTTATGAAGG
29881 TGAGAATGCC ACTCTAGTGG GCATCAGTGG TCAAAATGTC AGCTGGCTAA AATACCATCT
29941 AGATGGGTGG AAAGACATTT GCGATTGGAA TGTCACTGTG TATACATGTA ATGGAGTTAA
30001 CCTCACCATT ACTAATGCCA CCCAAGATCA GAATGGTAGG TTTAAGGGCC AGAGTTTCAC
30061 TAGAAATAAT GGGTATGAAT CCCATAACAT GTTTATCTAT GACGTCACTG TCATCAGAAA
30121 TGAGACTGCC ACCACCACAC AGATGCCCAC TACACACAGT TCTACCACTA CTACCATGCA
30181 AACCACACAG ACAACCACTA CATCAACTCA GCATATGACC ACCACTACAG CAGCAAAGCC
30241 AAGTAGTGCA GCGCCTCAGC CCCAGGCTTT GGCTTTGAAA GCTGCACAAC CTAGTACAAC
30301 TACTAGGACC AATGAGCAGA CTACTGAATT TTTGTCCACT GTCGAGAGCC ACACCACAGC
30361 TACCTCCAGT GCCTTCTCTA GCACCGCCAA TCTCTCCTCG CTTTCCTCTA CACCAATCAG
30421 TCCCGCTACT ACTCCCACCC CAGCTCTTCT CCCCACTCCC CTGAAGCAAA CTGAGGACAG
30481 CGGCATGCAA TGGCAGATCA CCCTGCTCAT TGTGATCGGG TTGGTCATCC TGGCCGTGTT
30541 GCTCTACTAC ATCTTCTGCC GCCGCATTCC CAACGCGCAC CGCAAACCGG CCTACAAGCC
30601 CATCGTTATC GGGCAGCCGG AGCCGCTTCA GGTGGAAGGG GGTCTAAGGA ATCTTCTCTT
30661 CTCTTTTACA GTATGGTGAT TGAACTATGA TTCCTAGACA ATTCTTGATC ACTATTCTTA
30721 TCTGCCTCCT CCAAGTCTGT GCCACCCTCG CTCTGGTGGC CAACGCCAGT CCAGACTGTA
30781 TTGGGCCCTT CGCCTCCTAC GTGCTCTTTG CCTTCATCAC CTGCATCTGC TGCTGTAGCA
30841 TAGTCTGCCT GCTTATCACC TTCTTCCAGT TCATTGACTG GATCTTTGTG CGCATCGCCT
30901 ACCTGCGCCA CCACCCCCAG TACCGCGACC AGCGAGTGGC GCGGCTGCTC AGGCTCCTCT
30961 GATAAGCATG CGGGCTCTGC TACTTCTCGC GCTTCTGCTG TTAGTGCTCC CCCGCCCCGT
31021 CGACCCCCGG TCCCCCACTC AGTCCCCCGA AGAGGTCCGC AAATGCAAAT TCCAAGAACC
31081 CTGGAAATTC CTCAAATGCT ACCGCCAAAA ATCAGACATG CTTCCCAGCT GGATCATGAT
31141 CATTGGGATC GTGAACATTC TGGCCTGCAC CCTCATCTCC TTTGTGATTT ACCCCTGCTT
31201 TGACTTTGGT TGGAACTCGC CAGAGGCGCT CTATCTCCCG CCTGAACCTG ACACACCACC
31261 ACAGCAACCT CAGGCACACG CACTACCACC ACCACAGCCT AGGCCACAAT ACATGCCCAT
31321 ATTAGACTAT GAGGCCGAGC CACAGCGACC CATGCTCCCC GCTATTAGTT ACTTCAATCT
31381 AACCGGCGGA GATGACTGAC CCACTGGCCA ACAACAACGT CAACGACCTT CTCCTGGACA
31441 TGGACGGCCG CGCCTCGGAG CAGCGACTCG CCCAACTTCG CATTCGCCAG CAGCAGGAGA
31501 GAGCCGTCAA GGAGCTGCAG GACGGCATAG CCATCCACCA GTGCAAGAAA GGCATCTTCT
31561 GCCTGGTGAA ACAGGCCAAG ATCTCCTACG AGGTCACCCC GACCGACCAT CGCCTCTCCT
31621 ACGAGCTCCT GCAGCAGCGC CAGAAGTTCA CCTGCCTGGT CGGAGTCAAC CCCATCGTCA
31681 TCACCCAGCA GTCGGGCGAT ACCAAGGGGT GCATCCACTG CTCCTGCGAC TCCCCCGACT
31741 GCGTCCACAC TCTGATCAAG ACCCTCTGCG GCCTCCGCGA CCTCCTCCCC ATGAACTAAT
31801 CACCCCCTTA TCCAGTGAAA TAAATATCAT ATTGATGATG ATTTAAATAA AAAATAATCA
31861 TTTGATTTGA AATAAAGATA CAATCATATT GATGATTTGA GTTTTAAAAA ATAAAGAATC
31921 ACTTACTTGA AATCTGATAC CAGGTCTCTG TCCATGTTTT CTGCCAACAC CACCTCACTC
31981 CCCTCTTCCC AGCTCTGGTA CTGCAGACCC CGGCGGGCTG CAAACTTCCT CCACACGCTG
32041 AAGGGGATGT CAAATTCCTC CTGTCCCTCA ATCTTCATTT TATCTTCTAT CAGATGTCCA
32101 AAAAGCGCGT CCGGGTGGAT GATGACTTCG ACCCCGTCTA CCCCTACGAT GCAGACAACG
32161 CACCGACCGT GCCCTTCATC AACCCCCCCT TCGTCTCTTC AGATGGATTC CAAGAGAAGC
32221 CCCTGGGGGT GCTGTCCCTG CGACTGGCTG ACCCCGTCAC CACCAAGAAC GGGGAAATCA
32281 CCCTCAAGCT GGGAGAGGGG GTGGACCTCG ACTCCTCGGG AAAACTCATC TCCAACACGG
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Fig. 8I

SEQ ID No: 4


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32341 CCACCAAGGC CGCCGCCCCT CTCAGTTTTT CCAACAACAC CATTTCCCTT AACATGGATA
32401 CCCCTCTTTA TACCAAAGAT GGAAAATTAT CCTTACAAGT TTCTCCACCG TTAAACATAT
32461 TAAAATCAAC CATTCTGAAC ACATTAGCTG TAGCTTATGG ATCAGGTTTA GGACTGAGTG
32521 GTGGCACTGC TCTTGCAGTA CAGTTGGCCT CTCCACTCAC TTTTGATGAA AAAGGAAATA
32581 TTAAAATTAA CCTAGCCAGT GGTCCATTAA CAGTTGATGC AAGTCGACTT AGTATCAACT
32641 GCAAAAGAGG GGTCACTGTC ACTACCTCAG GAGATGCAAT TGAAAGCAAC ATAAGCTGGC
32701 CTAAAGGTAT AAGATTTGAA GGTAATGGCA TAGCTGCAAA CATTGGCAGA GGATTGGAAT
32761 TTGGAACCAC TAGTACAGAG ACTGATGTCA CAGATGCATA CCCAATTCAA GTTAAATTGG
32821 GTACTGGCCT TACCTTTGAC AGTACAGGCG CCATTGTTGC TTGGAACAAA GAGGATGATA
32881 AACTTACATT ATGGACCACA GCCGACCCCT CGCCAAATTG CAAAATATAC TCTGAAAAAG
32941 ATGCCAAACT CACACTTTGC TTGACAAAGT GTGGAAGTCA AATTCTGGGT ACTGTGACTG
33001 TATTGGCAGT GAATAATGGA AGTCTCAACC CAATCACAAA CACAGTAAGC ACTGCACTCG
33061 TCTCCCTCAA GTTTGATGCA AGTGGAGTTT TGCTAAGCAG CTCCACATTA GACAAAGAAT
33121 ATTGGAACTT CAGAAAGGGA GATGTTACAC CTGCTGAGCC CTATACTAAT GCTATAGGTT
33181 TTATGCCTAA CATAAAGGCC TATCCTAAAA ACACATCTGC AGCTTCAAAA AGCCATATTG
33241 TCAGTCAAGT TTATCTCAAT GGGGATGAGG CCAAACCACT GATGCTGATT ATTACTTTTA
33301 ATGAAACTGA GGATGCAACT TGCACCTACA GTATCACTTT TCAATGGAAA TGGGATAGTA
33361 CTAAGTACAC AGGTGAAACA CTTGCTACCA GCTCCTTCAC CTTCTCCTAC ATCGCCCAAG
33421 AATGAACACT GTATCCCACC CTGCATGCCA ACCCTTCCCA CCCCACTCTG TCTATGGAAA
33481 AAACTCTGAA GCACAAAATA AAATAAAGTT CAAGTGTTTT ATTGATTCAA CAGTTTTACA
33541 GGATTCGAGC AGTTATTTTT CCTCCACCCT CCCAGGACAT GGAATACACC ACCCTCTCCC
33601 CCCGCACAGC CTTGAACATC TGAATGCCAT TGGTGATGGA CATGCTTTTG GTCTCCACGT
33661 TCCACACAGT TTCAGAGCGA GCCAGTCTCG GGTCGGTCAG GGAGATGAAA CCCTCCGGGC
33721 ACTCCCGCAT CTGCACCTCA CAGCTCAACA GCTGAGGATT GTCCTCGGTG GTCGGGATCA
33781 CGGTTATCTG GAAGAAGCAG AAGAGCGGCG GTGGGAATCA TAGTCCGCGA ACGGGATCGG
33841 CCGGTGGTGT CGCATCAGGC CCCGCAGCAG TCGCTGCCGC CGCCGCTCCG TCAAGCTGCT
33901 GCTCAGGGGG TCCGGGTCCA GGGACTCCCT CAGCATGATG CCCACGGCCC TCAGCATCAG
33961 TCGTCTGGTG CGGCGGGCGC AGCAGCGCAT GCGGATCTCG CTCAGGTCGC TGCAGTACGT
34021 GCAACACAGG ACCACCAGGT TGTTCAACAG TCCATAGTTC AACACGCTCC AGCCGAAACT
34081 CATCGCGGGA AGGATGCTAC CCACGTGGCC GTCGTACCAG ATCCTCAGGT AAATCAAGTG
34141 GCGCTCCCTC CAGAACACGC TGCCCACGTA CATGATCTCC TTGGGCATGT GGCGGTTCAC
34201 CACCTCCCGG TACCACATCA CCCTCTGGTT GAACATGCAG CCCCGGATGA TCCTGCGGAA
34261 CCACAGGGCC AGCACCGCCC CGCCCGCCAT GCAGCGAAGA GACCCCGGGT CCCGGCAATG
34321 GCAATGGAGG ACCCACCGCT CGTACCCGTG GATCATCTGG GAGCTGAACA AGTCTATGTT
34381 GGCACAGCAC AGGCATATGC TCATGCATCT CTTCAGCACT CTCAGCTCCT CGGGGGTCAA
34441 AACCATATCC CAGGGCACGG GGAACTCTTG CAGGACAGCG AACCCCGCAG AACAGGGCAA
34501 TCCTCGCACA TAACTTACAT TGTGCATGGA CAGGGTATCG CAATCAGGCA GCACCGGGTG
34561 ATCCTCCACC AGAGAAGCGC GGGTCTCGGT CTCCTCACAG CGTGGTAAGG GGGCCGGCCG
34621 ATACGGGTGA TGGCGGGACG CGGCTGATCG TGTTCGCGAC CGTGTCATGA TGCAGTTGCT
34681 TTCGGACATT TTCGTACTTG CTGTAGCAGA ACCTGGTCCG GGCGCTGCAC ACCGATCGCC
34741 GGCGGCGGTC CCGGCGCTTG GAACGCTCGG TGTTGAAATT GTAAAACAGC CACTCTCTCA
34801 GACCGTGCAG CAGATCTAGG GCCTCAGGAG TGATGAAGAT CCCATCATGC CTGATAGCTC
34861 TGATCACATC GACCACCGTG GAATGGGCCA GACCCAGCCA GATGATGCAA TTTTGTTGGG
34921 TTTCGGTGAC GGCGGGGGAG GGAAGAACAG GAAGAACCAT GATTAACTTT TAATCCAAAC
34981 GGTCTCGGAG CACTTCAAAA TGAAGGTCGC GGAGATGGCA CCTCTCGCCC CCGCTGTGTT
35041 GGTGGAAAAT AACAGCCAGG TCAAAGGTGA TACGGTTCTC GAGATGTTCC ACGGTGGCTT
35101 CCAGCAAAGC CTCCACGCGC ACATCCAGAA ACAAGACAAT AGCGAAAGCG GGAGGGTTCT
35161 CTAATTCCTC AATCATCATG TTACACTCCT GCACCATCCC CAGATAATTT TCATTTTTCC
35221 AGCCTTGAAT GATTCGAACT AGTTCCTGAG GTAAATCCAA GCCAGCCATG ATAAAGAGCT
35281 CGCGCAGAGC GCCCTCCACC GGCATTCTTA AGCACACCCT CATAATTCCA AGATATTCTG
35341 CTCCTGGTTC ACCTGCAGCA GATTGACAAG CGGAATATCA AAATCTCTGC CGCGATCCCT
35401 AAGCTCCTCC CTCAGCAATA ACTGTAAGTA CTCTTTCATA TCCTCTCCGA AATTTTTAGC
35461 CATAGGACCA CCAGGAATAA GATTAGGGCA AGCCACAGTA CAGATAAACC GAAGTCCTCC
35521 CCAGTGAGCA TTGCCAAATG CAAGACTGCT ATAAGCATGC TGGCTAGACC CGGTGATATC
35581 TTCCAGATAA CTGGACAGAA AATCACCCAG GCAATTTTTA AGAAAATCAA CAAAAGAAAA
35641 ATCCTCCAGG TGCACGTTTA GAGCCTCGGG AACAACGATG AAGTAAATGC AAGCGGTGCG
35701 TTCCAGCATG GTTAGTTAGC TGATCTGTAA AAAACAAAAA ATAAAACATT AAACCATGCT
35761 AGCCTGGCGA ACAGGTGGGT AAATCGTTCT CTCCAGCACC AGGCAGGCCA CGGGGTCTCC
35821 GGCGCGACCC TCGTAAAAAT TGTCGCTATG ATTGAAAACC ATCACAGAGA GACGTTCCCG
35881 GTGGCCGGCG TGAATGATTC GACAAGATGA ATACACCCCC GGAACATTGG CGTCCGCGAG
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Fig. 8J

SEQ ID No: 4

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35941 TGAAAAAAAG CGCCCGAGGA AGCAATAAGG CACTACAATG CTCAGTCTCA AGTCCAGCAA
36001 AGCGATGCCA TGCGGATGAA GCACAAAATC CTCAGGTGCG TACAAAATGT AATTACTCCC
36061 CTCCTGCACA GGCAGCGAAG CCCCCGATCC CTCCAGATAC ACATACAAAG CCTCAGCGTC
36121 CATAGCTTAC CGAGCAGCAG CACACAACAG GCGCAAGAGT CAGAGAAAGG CTGAGCTCTA
36181 ACCTGTCCAC CCGCTCTCTG CTCAATATAT AGCCCAGATC TACACTGACG TAAAGGCCAA
36241 AGTCTAAAAA TACCCGCCAA ATAATCACAC ACGCCCAGCA CACGCCCAGA AACCGGTGAC
36301 ACACTCAAAA AAATACGCGC ACTTCCTCAA ACGCCCAAAC TGCCGTCATT TCCGGGTTCC
36361 CACGCTACGT CATCGGAATT CGACTTTCAA ATTCCGTCGA CCGTTAAAAA CGTCACCCGC
36421 CCCGCCCCTA ACGGTCGCCC GTCTCTCGGC CAATCACCTT CCTCCCTCCC CAAATTCAAA
36481 CAGCTCATTT GCATATTAAC GCGCACCAAA AGTTTGAGGT ATATTATTGA TGATG
```

Fig. 8K

SEQ ID NO: 5


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  61 atttggggat gcggggcggt gattggctgc gggagcggcg accgttaggg gcggggcggg
 121 tgacgttttg atgacgtggc cgtgaggcgg agccggtttg caagttctcg tgggaaaagt
 181 gacgtcaaac gaggtgtggt ttgaacacgg aaatactcaa ttttcccgcg ctctctgaca
 241 ggaaatgagg tgtttctggg cggatgcaag tgaaaacggg ccattttcgc gcgaaaactg
 301 aatgaggaag tgaaaatctg agtaattccg cgtttatggc agggaggagt atttgccgag
 361 ggccgagtag actttgaccg attacgtggg ggtttcgatt accgtatttt tcacctaaat
 421 ttccgcgtac ggtgtcaaag tccggtgttt ttacgtaggt gtcagctgat cgccagggta
 481 tttaaacctg cgctctctag tcaagaggcc actcttgagt gccagcgagt agagttttct
 541 cctccgcgcc gcgagtcaga tctacacttt gaaagatgag gcacctgaga gacctgcccg
 601 gtaatgtttt cctggctact gggaacgaga ttctggaact ggtggtggac gccatgatgg
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1261 cagagtgcat ttcatcaccc ccagaaattg gcgaggaacc gcccgaagat attattcata
1321 gaccagttgc agtgagagtc accgggcgta gagcagctgt ggagagtttg gatgacttgc
1381 tacagggtgg ggatgaacct ttggacttgt gtacccggaa acgccccagg cactaagtgc
1441 cacacatgtg tgtttactta aggtgatgtc agtatttata gggtgtggag tgcaataaaa
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1621 aagactttca ccagactaga cagctgctag agaactcatc ggagggagtc tcttacctgt
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1741 aggatcaatt tgaggatatt ttgagagagt gtcctggtat ttttgactct ctcaacttgg
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2101 agcaagagga ggaccgagaa gagaacctga gagccggtct ggaccctccg gtggcggagg
2161 aggaggagta gctgacttgt ttcccgagct gcgccgggtg ctgactaggt cttccagtgg
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2461 gaggccagac aagaagtaca agattaccaa actgattaat atcagaaatt cctgctacat
2521 ttcagggaat ggggccgagg tggagatcag tacccaggag agggtggcct tcagatgctg
2581 catgatgaat atgtacccgg gggtggtggg catggaggga gtcaccttta tgaacgcgag
2641 gttcaggggt gatgggtata atggggtggt ctttatggcc aacaccaagc tgacagtgca
2701 cggatgctcc ttctttggct tcaataacat gtgcattgag gcctggggca gtgtttcagt
2761 gaggggatgc agtttttcag ccaactggat gggggtcgtg ggcagaacca agagcatggt
2821 gtcagtgaag aaatgcctgt tcgagaggtg ccacctgggg gtgatgagcg agggcgaagc
2881 caaagtcaaa cactgcgcct ctaccgagac gggctgcttt gtactgatca agggcaatgc
2941 caaagtcaag cataatatga tctgtggggc ctcggatgag cgcggctacc agatgctgac
3001 ctgcgccggt gggaacagcc atatgctagc caccgtgcat gtggcctcgc acccccgcaa
3061 gacatggccc gagttcgagc acaacgtcat gacccgctgc aatgtgcacc tggggtcccg
3121 ccgaggcatg ttcatgccct accagtgcaa catgcaattt gtgaaggtgc tgctggagcc
3181 cgatgccatg tccagagtga gcctgacggg ggtgtttgac atgaatgtgg agctgtggaa
3241 aattctgaga tatgatgaat ccaagaccag gtgccgggcc tgcgaatgcg gaggcaagca
3301 cgccaggctt cagcccgtgt gtgtggaggt gacggaggac ctgcgacccg atcatttggt
3361 gttgtcctgc aacgggacgg agttcggctc cagcggggaa gaatctgact agagtgagta
3421 gtgtttggga ctgggtggga gcctgcatga tgggcagaat gactaaaatc tgtgtttttc
```

Fig. 9A

SEQ ID NO: 5


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3481 tgcgcagcag catgagcgga agcgcctcct ttgagggagg ggtattcagc ccttatctga
3541 cggggcgtct cccctcctgg gcgggagtgc gtcagaatgt gatgggatcc acggtggacg
3601 gccggcccgt gcagcccgcg aactcttcaa ccctgaccta cgcgaccctg agctcctcgt
3661 ccgtggacgc agctgccgcc gcagctgctg cttccgccgc cagcgccgtg cgcggaatgg
3721 ccctgggcgc cggctactac agctctctgg tggccaactc gagttccacc aataatcccg
3781 ccagcctgaa cgaggagaag ctgctgctgc tgatggccca gctcgaggcc ctgacccagc
3841 gcctgggcga gctgacccag caggtggctc agctgcaggc ggagacgcgg gccgcggttg
3901 ccacggtgaa aaccaaataa aaaatgaatc aataaataaa cggagacggt tgttgatttt
3961 aacacagagt cttgaatctt tatttgattt ttcgcgcgcg gtaggccctg gaccaccggt
4021 ctcgatcatt gagcacccgg tggatctttt ccaggacccg gtagaggtgg gcttggatgt
4081 tgaggtacat gggcatgagc ccgtcccggg ggtggaggta gctccattgc agggcctcgt
4141 gctcgggggt ggtgttgtaa atcacccagt catagcaggg gcgcagggcg tggtgctgca
4201 cgatgtcctt gaggaggaga ctgatggcca cgggcagccc cttggtgtag gtgttgacga
4261 acctgttgag ctgggaggga tgcatgcggg gggagatgag atgcatcttg gcctggatct
4321 tgagattggc gatgttcccg cccagatccc gccgggggtt catgttgtgc aggaccacca
4381 gcacggtgta tccggtgcac ttggggaatt tgtcatgcaa cttggaaggg aaggcgtgaa
4441 agaatttgga gacgcccttg tgaccgccca ggttttccat gcactcatcc atgatgatgg
4501 cgatgggccc gtgggcggcg gcttgggcaa agacgtttcg ggggtcggac acatcgtagt
4561 tgtggtcctg ggtgagctcg tcataggcca ttttaatgaa tttggggcgg agggtgcccg
4621 actgggggac gaaggtgccc tcgatcccgg gggcgtagtt gccctcgcag atctgcatct
4681 cccaggcctt gagctcggag gggggatca tgtccacctg cggggcgatg aaaaaaacgg
4741 tttccggggc gggggagatg agctgggccg aaagcaggtt ccggagcagc tgggacttgc
4801 cgcagccggt ggggccgtag atgaccccga tgaccggctg caggtggtag ttgagggaga
4861 gacagctgcc gtcctcgcgg aggaggggcg ccacctcgtt catcatctcg cgcacatgca
4921 tgttctcgcg cacgagttcc gccaggaggc gctcgccccc aagcgagagg agctcttgca
4981 gcgaggcgaa gtttttcagc ggcttgagcc cgtcggccat gggcattttg gagagggtct
5041 gttgcaagag ttccagacgg tcccagagct cggtgatgtg ctctagggca tctcgatcca
5101 gcagacctcc tcgtttcgcg ggttggggcg actgcgggag tagggcacca ggcgatgggc
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5341 catgagttcg tagttgagcg cctcggccgc gtggcccttg gcgcggagct taccttttgga
5401 agtgtgtccg cagacgggac agaggaggga cttgagggcg tagagcttgg gggcgaggaa
5461 gacggactcg ggggcgtagg cgtccgcgcc gcagctggcg cagacggtct cgcactccac
5521 gagccaggtg aggtctggcc ggtcggggtc aaaaacgagg tttcctccgt gctttttgat
5581 gcgtttctta cctctggtct ccatgagctc gtgtccccgc tgggtgacaa agaggctgtc
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5821 gcacatgtcc ccctcgtcca catccaggaa ggtgattggc ttgtaagtgt aggccacgtg
5881 accgggggtc ccggccgggg gggtataaaa gggggcgggc ccctgctcgt cctcactgtc
5941 ttccggatcg ctgtccagga gcgccagctg ttggggtagg tattccctct cgaaggcggg
6001 catgacctcg gcactcaggt tgtcagtttc tagaaacgag gaggatttga tattgacggt
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6121 gttgtcgagc ttggtggcga aggagccgta gagggcgttg gagagcagct tggcgatgga
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6241 gtactcgcgc gccacgcact tccattcggg gaagacggtg gtgagcttgt cgggcacgat
6301 tctgacccgc cagccgcggt tgtgcagggt gatgaggtcc acgctggtgg ccacctcgcc
6361 gcgcaggggc tcgttggtcc agcagaggcg cccgcccttg cgcgagcaga agggggggcag
6421 cgggtccagc atgagctcgt cgggggggtc ggcgtccacg gtgaagatgc cgggcaggag
6481 ctcggggtcg aagtagctga tgcaggtgcc cagatcgtcc agcgccgctt gccagtcgcg
6541 cacggccagc gcgcgctcgt aggggctgag gggcgtgccc cagggcatgg ggtgcgtgag
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6661 gtaggtgggg tagcagcgcc ccccgcggat gctggcgcgc acgtagtcgt acagctcgtg
6721 cgagggcgcg aggagcccgg tgccgaggtt ggagcgctgc ggcttttcgg cgcggtagac
6781 gatctggcgg aagatggcgt gggagttgga ggagatggtg ggcctctgga agatgttgaa
6841 gtgggcgtgg ggcagtccga ccgagtccct gatgaagtgg gcgtaggagt cctgcagctt
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Fig. 9B

SEQ ID NO: 5


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 6901 ggcgacgagc tcggcggtga cgaggacgtc cagggcgcag tagtcgaggg tctcttggat
 6961 gatgtcgtac ttgagctggc ccttctgctt ccacagctcg cggttgagaa ggaactcttc
 7021 gcggtccttc cagtactctt cgaggggaa cccgtcctga tcggcacggt aagagcccac
 7081 catgtagaac tggttgacgg ccttgtaggc gcagcagccc ttctccacgg ggagggcgta
 7141 agcttgcgcg gccttgcgca gggaggtgtg ggtgagggcg aaggtgtcgc gcaccatgac
 7201 cttgaggaac tggtgcttga agtcgaggtc gtcgcagccg ccctgctccc agagctggaa
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 7381 gttgttgatg acctgggcgg cgaggacgat ctcgtcgaag ccgttgatgt tgtgcccgac
 7441 gatgtagagt tccacgaatc gcgggcggcc cttgacgtgg ggcagcttct tgagctcgtc
 7501 gtaggtgagc tcggcggggt cgctgaggcc gtgctgctcg agggcccagt cggcgaggtg
 7561 ggggttggcg ccgaggaagg aagtccagag atccacggcc agggcggtct gcaagcggtc
 7621 ccggtactga cggaactgct ggcccacggc catttttttcg ggggtgacgc agtagaaggt
 7681 gcgggggtcg ccgtgccagc ggtcccactt gagctggagg gcgaggtcgt gggcgagctc
 7741 gacgagcggc gggtccccgg agagtttcat gaccagcatg aaggggacga gctgcttgcc
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 7861 aggatgcgag ccgatgggga agaactggat ctcctgccac cagttggagg aatggctgtt
 7921 gatgtgatgg aagtagaaat gccgacggcg cgccgagcac tcgtgcttgt gtttatacaa
 7981 gcgtccgcag tgctcgcaac gctgcacggg atgcacgtgc tgcacgagct gtacctgggt
 8041 tcctttgacg aggaatttca gtgggcagtg gagcgctggc ggctgcatct ggtgctgtac
 8101 tacgtcctgg ccatcggcgt ggccatcgtc tgcctcgatg gtggtcatgc tgacgaggcc
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 8221 caggccggag ctgtccaggg tcctgagacg ctgcggagtc aggtcagtgg gcagcggcgg
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 9061 ctgacgtcgc ccagggcttc caagcgctcc atggcctcgt agaagtccac ggcgaagttg
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 9781 tggtcctgac acctggcgag gtccttgtag tagtcctgca tgagccgctc cacgggcacc
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10261 atccaggtga tgccggcggc ggtggtggag gcgcgcggga actcgcggac gcggttccag
10321 atgttgcgca gcggcaggaa gtagttcatg gtggccgcgg tctggcccgt gaggcgcgcg
10381 cagtcgtgga tgctctagac atacgggcaa aaacgaaagc ggtcagcggc tcgactccgt
```

Fig. 9C

```
10441 ggcctggagg ctaagcgaac gggttgggct gcgcgtgtac cccggttcga gtccctgctc
10501 gaatcaggct ggagccgcag ctaacgtggt actggcactc ccgtctcgac ccaagcctgc
10561 taacgaaacc tccaggatac ggaggcgggt cgttttggcc attttcgtca ggccggaaat
10621 gaaactagta agcgcggaaa gcggccgtcc gcgatggctc gctgccgtag tctggagaaa
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11101 cctacgtgcc caagcagaac ctgttcagag acaggagcgg cgaggagccc gaggagatgc
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11341 aaaaatcctt caacaaccac gtgcgcacgc tgatcgcgcg cgaggaggtg accctgggcc
11401 tgatgcacct gtgggacctg ctggaggcca tcgtgcagaa ccccacgagc aagccgctga
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11521 tgctgaatat caccgagccc gagggccgct ggctcctgga cctggtgaac attctgcaga
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11641 cggtgctgag cctgggcaag tactacgcta ggaagatcta caagaccccg tacgtgccca
11701 tagacaagga ggtgaagatc gacgggtttt acatgcgcat gaccctgaaa gtgctgaccc
11761 tgagcgacga tctgggggtg taccgcaacg acaggatgca ccgcgcggtg agcgccagcc
11821 gccggcgcga gctgagcgac caggagctga tgcacagcct gcagcgggcc ctgaccgggg
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11941 gccgggcctt ggaagctgcc ggcggttccc cctacgtgga ggaggtggac gatgaggagg
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13741 cagcgtgttg gacttgggtg ggagtggtgg tggtaacccg ttcgctcacc tgcgcccccg
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Fig. 9D

SEQ ID NO: 5

13861 cgaccagcgt gcgttcttct ctgttgtttg tagtagtatg atgaggcgcg tgtacccgga
13921 gggtcctcct ccctcgtacg agagcgtgat gcagcaggcg gtggcggcgg cgatgcagcc
13981 cccgctggag gcgccttacg tgcccccgcg gtacctggcg cctacggagg ggcggaacag
14041 cattcgttac tcggagctgg cacccttgta cgataccacc cggttgtacc tggtggacaa
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14221 cgagcgctcg cggtggggcg gccagctgaa aaccatcatg cacaccaaca tgcccaacgt
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15421 cacctgcccc tacgtctaca aggccctggg cgtagtcgcg ccgcgcgtcc tctcgagccg
15481 caccttctaa aaaatgtcca ttctcatctc gcccagtaat aacaccggtt ggggcctgcg
15541 cgcgcccagc aagatgtacg gaggcgctcg ccaacgctcc acgcaacacc ccgtgcgcgt
15601 gcgcgggcac ttccgcgctc cctggggcgc cctcaagggc cgcgtgcgct cgcgcaccac
15661 cgtcgacgac gtgatcgacc aggtggtggc cgacgcgcgc aactacacgc ccgccgccgc
15721 gcccgtctcc accgtggacg ccgtcatcga cagcgtggtg gccgacgcgc gccggtacgc
15781 ccgcgccaag agccggcggc ggcgcatcgc ccggcggcac cggagcaccc ccgccatgcg
15841 cgcggcgcga gccttgctgc gcagggccag gcgcacggga cgcagggcca tgctcagggc
15901 ggccagacgc gcggcctccg gcagcagcag cgccggcagg acccgcagac gcgcggccac
15961 ggcggcggcg gcggccatcg ccagcatgtc ccgcccgcgg cgcggcaacg tgtactgggt
16021 gcgcgacgcc gccaccggtg tgcgcgtgcc cgtgcgcacc cgccccctc gcacttgaag
16081 atgctgactt cgcgatgttg atgtgtccca gcggcgagga ggatgtccaa gcgcaaattc
16141 aaggaagaga tgctccaggt catcgcgcct gagatctacg gcccggcggc ggtgaaggag
16201 gaaagaaagc cccgcaaact gaagcgggtc aaaaaggaca aaaaggagga ggaagatgtg
16261 gacggactgg tggagtttgt gcgcgagttc gccccccggc ggcgcgtgca gtggcgcggg
16321 cggaaagtga aaccggtgct gcgacccggc accacggtgg tcttcacgcc cggcgagcgt
16381 tccggctccg cctccaagcg ctcctacgac gaggtgtacg gggacgagga catcctcgag
16441 caggcggccg aacgtctggg cgagtttgct tacggcaagc gcagccgccc cgcgcccttg
16501 aaagaggagg cggtgtccat cccgctggac cacggcaacc ccacgccgag cctgaagccg
16561 gtgaccctgc agcaggtgct gcctggtgcg gcgccgcgcc ggggcttcaa gcgcgagggc
16621 ggcgaggatc tgtacccgac catgcagctg atggtgccca agcgccagaa gctggaggac
16681 gtgctggagc acatgaaggt ggaccccgag gtgcagcccg aggtcaaggt gcggcccatc
16741 aagcaggtgg ccccgggcct gggcgtgcag accgtggaca tcaagatccc cacggagccc
16801 atggaaacgc agaccgagcc cgtgaagccc agcaccagca ccatggaggt gcagacggat
16861 ccctggatgc cggcaccggc ttccaccacc cgccgaagac gcaagtacgg cgcggccagc
16921 ctgctgatgc ccaactacgc gctgcatcct tccatcatcc ccacgccggg ctaccgcggc
16981 acgcgcttct accgcggcta caccagcagc cgccgccgca agaccaccac ccgccgccgc
17041 cgtcgtcgca cccgccgcag cagcaccgcg acttccgccg ccgccctggt gcggagagtg
17101 taccgcagcg ggcgcgagcc tctgaccctg ccgcgcgcgc gctaccaccc gagcatcgcc
17161 atttaactac cgcctcctac ttgcagatat ggccctcaca tgccgcctcc gcgtccccat
17221 tacgggctac cgaggaagaa agccgcgccg tagaaggctg acggggaacg ggctgcgtcg
17281 ccatcaccac cggcggcggc gcgccatcag caagcggttg gggggaggct tcctgcccgc
17341 gctgatgccc atcatcgccg cggcgatcgg ggcgatcccc ggcatagctt ccgtggcggt

Fig. 9E

SEQ ID NO: 5

```
17401 gcaggcctct cagcgccact gagacacagc ttggaaaatt tgtaataaaa aatggactga
17461 cgctcctggt cctgtgatgt gtgtttttag atggaagaca tcaatttttc gtccctggca
17521 ccgcgacacg gcacgcggcc gtttatgggc acctggagcg acatcggcaa cagccaactg
17581 aacgggggcg ccttcaattg gagcagtctc tggagcgggc ttaagaattt cgggtccacg
17641 ctcaaaacct atggcaacaa ggcgtggaac agcagcacag ggcaggcgct gagggaaaag
17701 ctgaaagagc agaacttcca gcagaaggtg gtcgatggcc tggcctcggg catcaacggg
17761 gtggtggacc tggccaacca ggccgtgcag aaacagatca acagccgcct ggacgcggtc
17821 ccgcccgcgg ggtccgtgga gatgccccag gtggaggagg agctgcctcc cctggacaag
17881 cgcggcgaca agcgaccgcg tcccgacgcg gaggagacgc tgctgacgca cacggacgag
17941 ccgccccgt acgaggaggc ggtgaaactg ggtctgccca ccacgcggcc cgtggcgcct
18001 ctggccaccg gggtgctgaa acccagcagc agcagcagcc agcccgcgac cctggacttg
18061 cctccgcctg cttcccgccc ctccacagtg gctaagcccc tgccgccggt ggccgtcgcg
18121 tcgcgcgccc cccgaggccg cccccaggcg aactggcaga gcactctgaa cagcatcgtg
18181 ggtctgggag tgcagagtgt gaagcgccgc cgctgctatt aaaagacact gtagcgctta
18241 acttgcttgt ctgtgtgtat atgtatgtcc gccgaccaga aggaggagga agaggcgcgt
18301 cgccgagttg caagatggcc accccatcga tgctgcccca gtgggcgtac atgcacatcg
18361 ccggacagga cgcttcggag tacctgagtc cgggtctggt gcagttcgcc cgcgccacag
18421 acacctactt cagtctgggg aacaagttta ggaaccccac ggtggcgccc acgcacgatg
18481 tgaccaccga ccgcagccag cggctgacgc tgcgcttcgt gcccgtggac cgcgaggaca
18541 acacctactc gtacaaagtg cgctacacgc tggccgtggg cgacaaccgc gtgctggaca
18601 tggccagcac ctactttgac atccgcggcg tgctggatcg gggccctagc ttcaaaccct
18661 actccggcac cgcttacaac agcctggctc ccaagggagc gcccaacact tgccagtgga
18721 catataaagc tgatggtgat actggtacag aaaaaaccta tacatatgga aatgcgcctg
18781 tgcaaggcat tagtattaca aaagatggta ttcaacttgg aactgacact gatgatcagc
18841 ccatttatgc agataaaact tatcaaccag agcctcaagt gggtgatgct gaatggcatg
18901 acatcactgg tactgatgaa aaatatggag gcagagctct caagcctgac accaaaatga
18961 agccctgcta tggttctttt gccaagccta ccaataaaga aggaggtcag gcaaatgtga
19021 aaaccgaaac aggcggtacc aaagaatatg acattgacat ggcattcttc gataatcgaa
19081 gtgcagctgc ggctggcctg gccccagaaa ttgttttgta tactgagaat gtggatctgg
19141 aaactccaga tactcatatt gtatacaagg cgggcacaga tgacagcagc tcttctatca
19201 atttgggtca gcagtccatg cccaacagac ccaactacat tggctttaga gacaacttta
19261 tcgggctcat gtactacaac agcactggca acatgggcgt gctggctggt caggcctccc
19321 agctgaatgc tgtggtggac ttgcaggaca gaaacactga actgtcctac cagctcttgc
19381 ttgactctct gggcgacaga accaggtatt tcagtatgtg gaatcaggcg gtggacagct
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19561 ctgatcaaac cacctggacc aaagatgata ctgttaatga tgctaatgaa ttgggcaagg
19621 gcaatccttt cgccatggag atcaacatcc aggccaacct gtggcggaac ttcctctacg
19681 cgaacgtggc gctgtacctg cccgactcct acaagtacac gccggccaac atcacgctgc
19741 cgaccaacac caacacctac gattacatga acggccgcgt ggtggcgccc tcgctggtgg
19801 acgcctacat caacatcggg gcgcgctggt cgctggaccc catggacaac gtcaaccct
19861 tcaaccacca ccgcaacgcg ggcctgcgct accgctccat gctcctgggc aacgggcgct
19921 acgtgccctt ccacatccag gtgccccaaa agttcttcgc catcaagagc ctcctgctcc
19981 tgcccgggtc ctacacctac gagtggaact tccgcaagga cgtcaacatg atcctgcaga
20041 gctccctcgg caacgacctg cgcacggacg gggcctccat cgccttcacc agcatcaacc
20101 tctacgccac cttcttcccc atggcgcaca acaccgcctc cacgctcgag gccatgctgc
20161 gcaacgacac caacgaccag tccttcaacg actacctctc ggcggccaac atgctctacc
20221 ccatcccggc caacgccacc aacgtgccca tctccatccc ctcgcgcaac tgggccgcct
20281 tccgcggatg gtccttcacg cgcctcaaga cccgcgagac gccctcgctc ggctccgggt
20341 tcgaccccta cttcgtctac tcgggctcca tcccctacct cgacggcacc ttctacctca
20401 accacacctt caagaaggtc tccatcacct tcgactcctc cgtcagctgg cccggcaacg
20461 accgcctcct gacgcccaac gagttcgaaa tcaagcgcac cgtcgacgga gaggggtaca
20521 acgtggccca gtgcaacatg accaaggact ggttcctggt ccagatgctg gcccactaca
20581 acatcggcta ccagggcttc tacgtgcccg agggctacaa ggaccgcatg tactccttct
20641 tccgcaactt ccagcccatg agccgccagg tcgtggacga ggtcaactac aaggactacc
20701 aggccgtcac cctggcctac cagcacaaca actcgggctt cgtcggctac ctcgcgccca
20761 ccatgcgcca gggacagccc taccccgcca actaccccta cccgctcatc ggcaagagcg
```

Fig. 9F

SEQ ID NO: 5


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20821 ccgtcgccag cgtcacccag aaaaagttcc tctgcgaccg ggtcatgtgg cgcatcccct
20881 tctccagcaa cttcatgtcc atgggcgcgc tcaccgacct cggccagaac atgctctacg
20941 ccaactccgc ccacgcgcta gacatgaatt tcgaagtcga ccccatggat gagtccaccc
21001 ttctctatgt tgtcttcgaa gtcttcgacg tcgtccgagt gcaccagccc caccgcggcg
21061 tcatcgaggc cgtctacctg cgcacgccct tctcggccgg caacgccacc acctaagccc
21121 cgctcttgct tcttgcaaga tgacggcctg tgcgggctcc ggcgagcagg agctcagggc
21181 catcctccgc gacctgggct gcgggccctg cttcctgggc accttcgaca agcgcttccc
21241 gggattcatg gccccgcaca agctggcctg cgccatcgtc aacacggccg gccgcgagac
21301 cgggggcgag cactggctgg ccttcgcctg gaacccgcgc tcccacacct gctacctctt
21361 cgaccccttc gggttctcgg acgagcgcct caagcagatc taccagttcg agtacgaggg
21421 cctgctgcgc cgcagcgccc tggccaccga ggaccgctgc gtcaccctgg aaaagtccac
21481 ccagaccgtg cagggtccgc gctcggccgc ctgcgggctc ttctgctgca tgttcctgca
21541 cgccttcgtg cactggcccg accgccccat ggacaagaac cccaccatga acttgctgac
21601 gggggtgccc aacggcatgc tccagtcgcc ccaggtggaa cccaccctgc gccgcaacca
21661 ggaggcgctc taccgcttcc tcaacgccca ctccgcctac tttcgctccc accgcgcgcg
21721 catcgagaag gccaccgcct tcgaccgcat gaatcaagac atgtaaaccg tgtgtgtatg
21781 tgaatgcttt attcataata aacagcacat gtttatgcca ccttttctga ggctctgact
21841 ttatttagaa atcgaagggg ttctgccggc tctcggcgtg ccccgcgggc agggatacgt
21901 tgcggaactg gtacttgggc agccacttga actcggggat cagcagcttc ggcacgggga
21961 ggtcggggaa cgagtcgctc cacagcttgc gcgtgagttg cagggcgccc agcaggtcgg
22021 gcgcggagat cttgaaatcg cagttgggac ccgcgttctg cgcgcgggag ttgcggtaca
22081 cggggttgca gcactggaac accatcaggg ccgggtgctt cacgctcgcc agcaccgtcg
22141 cgtcggtgat gccctccacg tccagatcct cggcgttggc catcccgaag ggggtcatct
22201 tgcaggtctg ccgccccatg ctgggcacgc agccgggctt gtggttgcaa tcgcagtgca
22261 gggggatcag catcatctgg gcctgctcgg agctcatgcc cgggtacatg gccttcatga
22321 aagcctccag ctggcggaag gcctgctgcg ccttgccgcc ctcggtgaag aagaccccgc
22381 aggacttgct agagaactgg ttggtggcgc agccggcgtc gtgcacgcag cagcgcgcgt
22441 cgttgttggc cagctgcacc acgctgcgcc cccagcggtt ctgggtgatc ttggcccggt
22501 cggggttctc cttcagcgcg cgctgcccgt tctcgctcgc cacatccatc tcgatcgtgt
22561 gctccttctg gatcatcacg gtcccgtgca ggcatcgcag cttgccctcg gcctcggtgc
22621 acccgtgcag ccacagcgcg cagccggtgc actcccagtt cttgtgggcg atctgggagt
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22801 acacctcgcc ctgctcgggc atcagctgga aggcggactt caggtcgctc tccacgcggt
22861 accggtccat cagcagcgtc atgacttcca tgcccttctc ccaggccgag acgatcggca
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22981 cgttctcgtc cagggtctca aacactcgct tgccgtcctt ctcggtgatg cgcacggggg
23041 gaaagctgaa gcccacggcc gccagctcct cctcggcctg cctttcgtcc tcgctgtcct
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23521 acgccgccgc ggccccagac atgcaagaga tggaggaatc catcgagatt gacctgggct
23581 acgtgacgcc cgcggagcac gaggaggagc tggcagcgcg cttttcagcc ccggaagaga
23641 accaccaaga gcagccagag caggaagcag agagcgagca gcagcaggct gggctcgagc
23701 atggcgacta cctgagcggg gcagaggacg tgctcatcaa gcatctggcc cgccaatgca
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23821 gccgcgccta cgagcgcaac ctcttctcgc cgcgcgtgcc ccccaagcgc cagcccaacg
23881 gcacctgcga gcccaacccg cgcctcaact tctacccggt cttcgcggtg cccgaggccc
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24001 gcacccgcgc cgacgccctg ctcaacctgg gtcccggcgc ccgcctacct gatatcgcct
24061 ccttggaaga ggttcccaag atcttcgagg gtctgggcag cgacgagact cgggccgcga
24121 acgctctgca aggaagcgga gaggagcatg agcaccacag cgccctggtg gagttggaag
24181 gcgacaacgc gcgcctggcg gtgctcaagc gcacggtcga gctgacccac ttcgcctacc
24241 cggcgctcaa cctgcccccc aaggtcatga gcgccgtcat ggaccaggtg ctcatcaagc
24301 gcgcctcgcc cctctcggat gaggacatgc aggaccccga gagctcggac gagggcaagc
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Fig. 9G

SEQ ID NO: 5


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24361 ccgtggtcag cgacgagcag ctggcgcgct ggctgggagc gagtagcacc ccccagagct
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24481 tgcgccgctt cttcgccgac gcagagaccc tgcgcaaggt cgaggagaac ctgcactacc
24541 tcttcaggca cgggtttgtg cgccaggcct gcaagatctc caacgtggag ctgaccaacc
24601 tggtctccta catgggcatc ctgcacgaga accgcctggg gcagaacgtg ctgcacacca
24661 ccctgcgcgg ggaggcccgc cgcgactaca tccgcgactg cgtctacctg tacctctgcc
24721 acacctggca gacgggcatg ggcgtgtggc agcagtgcct ggaggagcag aacctgaaag
24781 agctctgcaa gctcctgcag aagaacctga aggccctgtg gaccgggttc gacgagcgca
24841 ccaccgcctc ggacctggcc gacctcatct tccccgagcg cctgcggctg acgctgcgca
24901 acggactgcc cgactttatg agtcaaagca tgttgcaaaa ctttcgctct ttcatcctcg
24961 aacgctccgg gatcctgccc gccacctgct ccgcgctgcc ctcggacttc gtgccgctga
25021 ccttccgcga gtgccccccg ccgctctgga gccactgcta cctgctgcgc ctggccaact
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25141 actgccgctg caacctctgc acgccgcacc gctccctggc ctgcaacccc cagctgctga
25201 gcgagaccca gatcatcggc accttcgagt tgcaaggccc cggcgagggc aaggggggtc
25261 tgaaactcac cccggggctg tggacctcgg cctacttgcg caagttcgtg cccgaggact
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25381 cggcctgcgt catcacccag ggggccatcc tggcccaatt gcaagccatc cagaaatccc
25441 gccaagaatt tctgctgaaa aagggccacg gggtctacct ggacccccag accggagagg
25501 agctcaaccc cagcttcccc caggatgccc cgaggaagca gcaagaagct gaaagtggag
25561 ctgccgccgc cggaggattt ggaggaagac tgggagagca gtcaggcaga ggaggaggag
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25681 gaggtggagg aggaggcaga ggaagaagca gccgccgcca gaccgtcgtc ctcggcggag
25741 aaagcaagca gcacggatac catctccgct ccgggtcggg gtcgcggcga ccgggcccac
25801 agtaggtggg acgagaccgg gcgcttcccg aaccccacca cccagaccgg taagaaggag
25861 cggcagggat acaagtcctg gcgggggcac aaaaacgcca tcgtctcctg cttgcaagcc
25921 tgcgggggca acatctcctt cacccgccgc tacctgctct tccaccgcgg ggtgaacttc
25981 ccccgcaaca tcttgcatta ctaccgtcac ctccacagcc cctactactg tttccaagaa
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26161 ccggatcttt cccaccctct atgccatctt ccagcagagt cgggggcagg agcaggaact
26221 gaaagtcaag aaccgttctc tgcgctcgct cacccgcagt tgtctgtatc acaagagcga
26281 agaccaactt cagcgcactc tcgaggacgc cgaggctctc ttcaacaagt actgcgcgct
26341 cactcttaaa gagtagcccg cgcccgccca cacacggaaa aaggcgggaa ttacgtcacc
26401 acctgcgccc ttcgcccgac catcatcatg agcaaagaga ttcccacgcc ttacatgtgg
26461 agctaccagc cccagatggg cctggccgcc ggcgccgccc aggactactc cacccgcatg
26521 aactggctca gcgccgggcc cgcgatgatc tcacgggtga atgacatccg cgcccgccga
26581 aaccagatac tcctagaaca gtcagcgatc accgccacgc cccgccatca ccttaatccg
26641 cgtaattggc ccgccgccct ggtgtaccag gaaattcccc agcccacgac cgtactactt
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26941 gagagttcgt cctcgcagcc ccgctcgggt ggcatcggca ctctccagtt cgtggaggag
27001 ttcactccct cggtctactt caaccccttc tccggctccc ccggccacta cccggacgag
27061 ttcatcccga acttcgacgc catcagcgag tcggtggacg gctacgattg aatgtcccat
27121 ggtggcgcag ctgacctagc tcggcttcga cacctggacc actgtcgcct ctcctacgag
27181 ctcctgcagc agcgccagaa gttcacctgc ctggtcggag tcaaccccat cgtcatcacc
27241 cagcagtcgg gcgataccaa ggggtgcatc cactgctcct gcgactcccc cgactgcgtc
27301 cacactctga tcaagaccct ctgcggcctc cgcgacctcc tccccatgaa ctaatcaccc
27361 ccttatccag tgaaataaag atcatattga tgatttgagt ttaataaaaa taaagaatca
27421 cttacttgaa atctgatacc aggtctctgt ccatgttttc tgccaacacc acttcactcc
27481 cctcttccca gctctggtac tgcaggcccc ggcgggctgc aaacttcctc cacaccctga
27541 aggggatgtc aaattcctcc tgtccctcaa tcttcatttt atcttctatc agatgtccaa
27601 aaagcgcgtc cgggtggatg atgacttcga ccccgtctac ccctacgatg cagacaacgc
27661 accgaccgtg cccttcatca acccccccct cgtctcttca gatggattcc aagagaagcc
27721 cctgggggtg ctgtccctgc gtctggccga tcccgtcacc accaagaacg gggaaatcac
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Fig. 9H

SEQ ID NO: 5


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27781 cctcaagctg ggagatgggg tggacctcga ctcctcggga aaactcatct ccaacacggc
27841 caccaaggcc gccgcccctc tcagtttttc caacaacacc atttcccttа acatggatac
27901 ccctttttac aacaacaatg gaaagttagg catgaaagtc actgctccac tgaagatact
27961 agacacagac ttgctaaaaa cacttgttgt agcttatgga caaggtttag gaacaaacac
28021 cactggtgcc cttgttgccc aactagcatc cccacttgct tttgatagca atagcaaaat
28081 tgcccttaat ttaggcaatg gaccattgaa agtggatgca aatagactga acatcaattg
28141 caatagagga ctctatgtta ctaccacaaa agatgcactg gaagccaata taagttgggc
28201 taatgctatg acatttatag gaaatgccat gggtgtcaat attgatacac aaaaaggctt
28261 gcaatttggc accactagta ccgtcgcaga tgttaaaaac gcttacccca tacaaatcaa
28321 acttggagct ggtctcacat ttgacagcac aggtgcaatt gttgcatgga acaaagatga
28381 tgacaagctt acactatgga ccacagccga ccctctcca aattgtcaca tatattctga
28441 aaaggatgct aagcttacac tttgcttgac aaagtgtggc agtcagattc tgggcactgt
28501 ttccctcata gctgttgata ctggcagttt aaatcccata acaggaacag taaccactgc
28561 tcttgtctca cttaaattcg atgcaaatgg agttttgcaa agcagctcaa cactagactc
28621 agactattgg aatttcagac agggagatgt tacacctgct gaagcctata ctaatgctat
28681 aggtttcatg cccaatctaa aagcataccc taaaaacaca agtggagctg caaaaagtca
28741 cattgttggg aaagtgtacc tacatgggga tacaggcaaa ccactggacc tcattattac
28801 tttcaatgaa acaagtgatg aatcttgcac ttactgtatt aactttcaat ggcagtgggg
28861 ggctgatcaa tataaaaatg aaacacttgc cgtcagttca ttcacctttt cctatattgc
28921 taaagaataa accccactct gtaccccatc tctgtctatg gaaaaaactc tgaaacacaa
28981 aataaaataa agttcaagtg ttttattgat tcaacagttt tacaggattc gagcagttat
29041 ttttcctcca ccctcccagg acatggaata caccaccctc tccccccgca cagccttgaa
29101 catctgaatg ccattggtga tggacatgct tttggtctcc acgttccaca cagtttcaga
29161 gcgagccagt ctcgggtcgg tcagggagat gaaaccctcc gggcactccc gcatctgcac
29221 ctcacagctc aacagctgag gattgtcctc ggtggtcggg atcacggtta tctggaagaa
29281 gcagaagagc ggcggtggga atcatagtcc gcgaacggga tcggccggtg gtgtcgcatc
29341 aggccccgca gcagtcgctg tcgccgccgc tccgtcaagc tgctgctcag ggggtccggg
29401 tccagggact ccctcagcat gatgcccacg gccctcagca tcagtcgtct ggtgcggcgg
29461 gcgcagcagc gcatgcggat ctcgctcagg tcgctgcagt acgtgcaaca caggaccacc
29521 aggttgttca acagtccata gttcaacacg ctccagccga aactcatcgc gggaaggatg
29581 ctacccacgt ggccgtcgta ccagatcctc aggtaaatca agtggcgccc cctccagaac
29641 acgctgccca tgtacatgat ctccttgggc atgtggcggt tcaccacctc ccggtaccac
29701 atcaccctct ggttgaacat gcagccccgg atgatcctgc ggaaccacag ggccagcacc
29761 gccccgcccg ccatgcagcg aagagacccc gggtcccgac aatggcaatg gaggacccac
29821 cgctcgtacc cgtggatcat ctgggagctg aacaagtcta tgttggcaca gcacaggcat
29881 atgctcatgc atctcttcag cactctcagc tcctcggggg tcaaaaccat atcccagggc
29941 acggggaact cttgcaggac agcgaacccc gcagaacagg gcaatcctcg cacataactt
30001 acattgtgca tggacagggt atcgcaatca ggcagcaccg ggtgatcctc caccagagaa
30061 gcgcgggtct cggtctcctc acagcgtggt aaggggccg gccgatacgg gtgatggcgg
30121 gacgcggctg atcgtgttcg cgaccgtgtt atgatgcagt tgctttcgga cattttcgta
30181 cttgctgtag cagaacctgg tccgggcgct gcacaccgat cgccggcggc ggtcccggcg
30241 cttggaacgc tcggtgttga agttgtaaaa cagccactct ctcagaccgt gcagcagatc
30301 tagggcctca ggagtgatga agatcccatc atgcctgatg gctctaatca catcgaccac
30361 cgtggaatgg gccagaccca gccagatgat gcaatttttgt tgggtttcgg tgacggcggg
30421 ggagggaaga acaggaagaa ccatgattaa cttttaatcc aaacggtctc ggagcacttc
30481 aaaatgaaga tcgcggagat ggcacctctc gcccccgctg tgttggtgga aaataacagc
30541 caggtcaaag gtgatacggt tctcgagatg ttccacggtg gcttccagca aagcctccac
30601 gcgcacatcc agaaacaaga caatagcgaa agcgggaggg ttctctaatt cctcaatcat
30661 catgttacac tcctgcacca tccccagata attttcattt ttccagcctt gaatgattcg
30721 aactagttcc tgaggtaaat ccaagccagc catgataaag agctcgcgca gagcgccctc
30781 caccggcatt cttaagcaca ccctcataat tccaagatat tctgctcctg gttcacctgc
30841 agcagattga caagcggaat atcaaaatct ctgccgcgat ccctaagctc ctccctcagc
30901 aataactgta agtactcttt catatcctct ccgaaatttt tagccatagg accaccagga
30961 ataagattag ggcaagccac agtacagata aaccgaagtc ctccccagtg agcattgcca
31021 aatgcaagac tgctataagc atgctggcta gacccggtga tatcttccag ataactggac
31081 agaaaatcgc ccaggcaatt tttaagaaaa tcaacaaaag aaaaatcctc caggtgcacg
```

Fig. 9I

SEQ ID NO: 5


```
31141 tttagagcct cgggaacaac gatggagtaa atgcaagcgg tgcgttccag catggttagt
31201 tagctgatct gtagaaaaaa acaaaaatga acattaaacc atgctagcct ggcgaacagg
31261 tgggtaaatc gttctctcca gcaccaggca ggccacgggg tctccggcac gaccctcgta
31321 aaaattgtcg ctatgattga aaaccatcac agagagacgt tcccggtggc cggcgtgaat
31381 gattcgacaa gatgaataca cccccggaac attggcgtcc gcgagtgaaa aaaagcgccc
31441 aaggaagcaa taaggcacta caatgctcag tctcaagtcc agcaaagcga tgccatgcgg
31501 atgaagcaca aaattctcag gtgcgtacaa aatgtaatta ctcccctcct gcacaggcag
31561 caaagccccc gatccctcca ggtacacata caaagcctca gcgtccatag cttaccgagc
31621 agcagcacac aacaggcgca agagtcagag aaaggctgag ctctaacctg tccacccgct
31681 ctctgctcaa tatatagccc agatctacac tgacgtaaag gccaaagtct aaaaataccc
31741 gccaaataat cacacacgcc cagcacacgc ccagaaaccg gtgacacact caaaaaaata
31801 cgcgcacttc ctcaaacgcc caaactgccg tcatttccgg gttcccacgc tacgtcatca
31861 aaattcgact ttcaaattcc gtcgaccgtt aaaaacgtcg cccgccccgc ccctaacggt
31921 cgccgctccc gcagccaatc accgccccgc atccccaaat tcaaatacct catttgcata
31981 ttaacgcgca ccaaaagttt gaggtatatt attgatgatg
```

Fig. 9J

```
       1  ATGAAGCGCA CCAAAACGTC TGACGAGAGC TTCAACCCCG TGTACCCCTA
TGACACGGAA

      61  AGCGGCCCTC CCTCCGTCCC TTTCCTCACC CCTCCCTTCG TGTCTCCCGA
TGGATTCCAA

     121  GAAAGTCCCC CCGGGGTCCT GTCTCTGAAC CTGGCCGAGC CCCTGGTCAC
TTCCCACGGC

     181  ATGCTCGCCC TGAAAATGGG AAGTGGCCTC TCCCTGGACG ACGCTGGCAA
CCTCACCTCT

     241  CAAGATATCA CCACCGCTAG CCCTCCCCTC AAAAAAACCA AGACCAACCT
CAGCCTAGAA

     301  ACCTCATCCC CCCTAACTGT GAGCACCTCA GGCGCCCTCA CCGTAGCAGC
CGCCGCTCCC

     361  CTGGCGGTGG CCGGCACCTC CCTCACCATG CAATCAGAGG CCCCCCTGAC
AGTACAGGAT

     421  GCAAAACTCA CCCTGGCCAC CAAAGGCCCC CTGACCGTGT CTGAAGGCAA
ACTGGCCTTG

     481  CAAACATCGG CCCCGCTGAC GGCCGCTGAC AGCAGCACCC TCACAGTCAG
TGCCACACCA

     541  CCCCTTAGCA CAAGCAATGG CAGCTTGGGT ATTGACATGC AAGCCCCCAT
TTACACCACC

     601  AATGGAAAAC TAGGACTTAA CTTTGGCGCT CCCCTGCATG TGGTAGACAG
CCTAAATGCA

     661  CTGACTGTAG TTACTGGCCA AGGTCTTACG ATAAACGGAA CAGCCCTACA
AACTAGAGTC

     721  TCAGGTGCCC TCAACTATGA CACATCAGGA AACCTAGAAT TGAGAGCTGC
AGGGGGTATG

     781  CGAGTTGATG CAAATGGTCA ACTTATCCTT GATGTAGCTT ACCCATTTGA
TGCACAAAAC

     841  AATCTCAGCC TTAGGCTTGG ACAGGGACCC CTGTTTGTTA ACTCTGCCCA
CAACTTGGAT

     901  GTTAACTACA ACAGAGGCCT CTACCTGTTC ACATCTGGAA ATACCAAAAA
GCTAGAAGTT

     961  AATATCAAAA CAGCCAAGGG TCTCATTTAT GATGACACTG CTATAGCAAT
CAATGCGGGT

    1021  GATGGGCTAC AGTTTGACTC AGGCTCAGAT ACAAATCCAT TAAAAACTAA
ACTTGGATTA

    1081  GGACTGGATT ATGACTCCAG CAGAGCCATA ATTGCTAAAC TGGGAACTGG
CCTAAGCTTT
```

Fig. 10A

SEQ ID NO: 6

1141 GACAACACAG GTGCCATCAC AGTAGGCAAC AAAAATGATG ACAAGCTCAC CTTGTGGACC

1201 ACACCAGACC CATCTCCTAA CTGTAGAATC TATTCAGAGA AAGATGCTAA ATTCACACTT

1261 GTTTTGACTA AATGCGGCAG TCAGGTGTTG GCCAGCGTTT CTGTTTTATC TGTAAAAGGT

1321 AGCCTTGCGC CCATCAGTGG CACAGTAACT AGTGCTCAGA TTGTCCTCAG ATTTGATGAA

1381 AATGGAGTTC TACTAAGCAA TTCTTCCCTT GACCCTCAAT ACTGGAACTA CAGAAAAGGT

1441 GACCTTACAG AGGGCACTGC ATATACCAAC GCAGTGGGAT TTATGCCCAA CCTCACAGCA

1501 TACCCAAAAA CACAGAGCCA AACTGCTAAA AGCAACATTG TAAGTCAGGT TTACTTGAAT

1561 GGGGACAAAT CCAAACCCAT GACCCTCACC ATTACCCTCA ATGGAACTAA TGAAACAGGA

1621 GATGCCACAG TAAGCACTTA CTCCATGTCA TTCTCATGGA ACTGGAATGG AAGTAATTAC

1681 ATTAATGAAA CGTTCCAAAC CAACTCCTTC ACCTTCTCCT ACATCGCCCA AGAATAA

Fig. 10B

```
      1  ATGTCCAAAA AGCGCGTCCG GGTGGATGAT GACTTCGACC CCGTCTACCC
CTACGATGCA

     61  GACAACGCAC CGACCGTGCC CTTCATCAAC CCCCCCTTCG TCTCTTCAGA
TGGATTCCAA

    121  GAGAAGCCCC TGGGGGTGTT GTCCCTGCGA CTGGCCGACC CCGTCACCAC
CAAGAACGGG

    181  GAAATCACCC TCAAGCTGGG AGAGGGGGTG GACCTCGATT CCTCGGGAAA
ACTCATCTCC

    241  AACACGGCCA CCAAGGCCGC CGCCCCTCTC AGTTTTTCCA ACAACACCAT
TTCCCTTAAC

    301  ATGGATCACC CCTTTTACAC TAAAGATGGA AAATTATCCT TACAAGTTTC
TCCACCATTA

    361  AATATACTGA GAACAAGCAT TCTAAACACA CTAGCTTTAG GTTTTGGATC
AGGTTTAGGA

    421  CTCCGTGGCT CTGCCTTGGC AGTACAGTTA GTCTCTCCAC TTACATTTGA
TACTGATGGA

    481  AACATAAAGC TTACCTTAGA CAGAGGTTTG CATGTTACAA CAGGAGATGC
AATTGAAAGC

    541  AACATAAGCT GGGCTAAAGG TTTAAAATTT GAAGATGGAG CCATAGCAAC
CAACATTGGA

    601  AATGGGTTAG AGTTTGGAAG CAGTAGTACA GAAACAGGTG TTGATGATGC
TTACCCAATC

    661  CAAGTTAAAC TTGGATCTGG CCTTAGCTTT GACAGTACAG GAGCCATAAT
GGCTGGTAAC

    721  AAAGAAGACG ATAAACTCAC TTTGTGGACA ACACCTGATC CATCACCAAA
CTGTCAAATA

    781  CTCGCAGAAA ATGATGCAAA ACTAACACTT TGCTTGACTA AATGTGGTAG
TCAAATACTG

    841  GCCACTGTGT CAGTCTTAGT TGTAGGAAGT GGAAACCTAA ACCCCATTAC
TGGCACCGTA

    901  AGCAGTGCTC AGGTGTTTCT ACGTTTTGAT GCAAACGGTG TTCTTTTAAC
AGAACATTCT

    961  ACACTAAAAA AATACTGGGG GTATAGGCAG GGAGATAGCA TAGATGGCAC
TCCATATACC

   1021  AATGCTGTAG GATTCATGCC CAATTTAAAA GCTTATCCAA AGTCACAAAG
TTCTACTACT

   1081  AAAAATAATA TAGTAGGGCA AGTATACATG AATGGAGATG TTTCAAAACC
TATGCTTCTC
```

Fig. 11A

1141 ACTATAACCC TCAATGGTAC TGATGACAGC AACAGTACAT ATTCAATGTC ATTTTCATAC

1201 ACCTGGACTA ATGGAAGCTA TGTTGGAGCA ACATTTGGGG CTAACTCTTA TACCTTCTCA

1261 TACATCGCCC AAGAATGA

Fig. 11B

```
        1  ATGTCCAAAA AGCGCGTCCG GGTGGATGAT GACTTCGACC CCGTCTACCC
CTACGATGCA

       61  GACAACGCAC CGACCGTGCC CTTCATCAAC CCCCCCTTCG TCTCTTCAGA
TGGATTCCAA

      121  GAGAAGCCCC TGGGGGTGCT GTCCCTGCGT CTGGCCGATC CCGTCACCAC
CAAGAACGGG

      181  GAAATCACCC TCAAGCTGGG AGATGGGGTG GACCTCGACG ACTCGGGAAA
ACTCATCTCC

      241  AACACGGCCA CCAAGGCCGC CGCCCCTCTC AGTTTTTCCA ACAACACCAT
TTCCCTTAAC

      301  ATGGATACCC CTCTTTACAA CAACAATGGA AAGCTAGGTA TGAAGGTAAC
CGCACCATTA

      361  AAGATATTAG ACACAGATCT ACTAAAAACA CTTGTTGTTG CTTATGGGCA
GGGATTAGGA

      421  ACAAACACCA ATGGTGCTCT TGTTGCCCAA CTAGCATACC CACTTGTTTT
TAATACCGCT

      481  AGCAAAATTG CCCTTAATTT AGGCAATGGA CCATTAAAAG TGGATGCAAA
TAGACTGAAC

      541  ATTAATTGCA AAAGAGGTAT CTATGTCACT ACCACAAAAG ATGCACTGGA
GATTAATATC

      601  AGTTGGGCAA ATGCTATGAC ATTTATAGGA AATGCCATTG GTGTCAATAT
TGACACAAAA

      661  AAAGGCCTAC AGTTCGGCAC TTCAAGCACT GAAACAGATG TTAAAAATGC
TTTTTCACTC

      721  CAAGTAAAAC TTGGAGCTGG TCTTACATTT GACAGCACAG GTGCCATTGT
TGCTTGGAAC

      781  AAAGAAGATG ACAAACTTAC ACTGTGGACC ACAGCCGATC CATCTCCAAA
CTGTCACATA

      841  TATTCTGCAA AGGATGCTAA GCTTACACTC TGCTTGACAA AGTGTGGTAG
TCAAATCCTA

      901  GGCACTGTCT CCCTATTAGC AGTCAGTGGC AGCTTGGCTC CTATCACAGG
GGCTGTTAGA

      961  ACTGCACTTG TATCACTCAA ATTCAATGCT AATGGAGCCC TTTTGGACAA
ATCAACTCTG

     1021  AACAAAGAAT ACTGGAACTA CAGACAAGGA GATCTAATTC CAGGTACACC
ATATACACAT

     1081  GCTGTGGGTT TCATGCCTAA CAAAAAAGCC TACCCTAAAA ACACAACTGC
AGCTTCCAAG
```

Fig. 12A

1141 AGCCACATTG TGGGTGATGT GTATTTAGAT GGAGATGCAG ATAAACCTTT ATCTCTTATC

1201 ATCACTTTCA ATGAAACTGA TGATGAAACC TGTGATTACT GCATCAACTT TCAATGGAAA

1261 TGGGGAGCTG ATCAATATAA GGATAAGACA CTCGCAACCA GTTCATTCAC CTTCTCATAC

1321 ATCGCCCAAG AATAA

Fig. 12B

1 ATGTCCAAAA AGCGCGTCCG GGTGGATGAT GACTTCGACC CCGTCTACCC CTACGATGCA

61 GACAACGCAC CGACCGTGCC CTTCATCAAC CCCCCCTTCG TCTCTTCAGA TGGATTCCAA

121 GAGAAGCCCC TGGGGGTGCT GTCCCTGCGA CTGGCCGACC CCGTCACCAC CAAGAACGGG

181 GAAATCACCC TCAAGCTGGG AGAGGGGGTG GACCTCGACT CCTCGGGAAA ACTCATCTCC

241 AACACGGCCA CCAAGGCCGC CGCCCCTCTC AGTTTTTCCA ACAACACCAT TTCCCTTAAC

301 ATGGATACCC CTTTTTACAA CAATAATGGA AAGTTAGGCA TGAAAGTCAC TGCTCCACTG

361 AAGATACTCG ACACAGACTT GCTAAAAACA CTTGTTGTAG CTTATGGACA AGGTTTAGGA

421 ACAAACACCA CTGGTGCCCT TGTTGCCCAA CTAGCAGCCC CACTTGCTTT TGATAGCAAT

481 AGCAAAATTG CCCTTAATTT AGGCAATGGA CCATTGAAAG TGGATGCAAA TAGACTGAAC

541 ATCAATTGCA ATAGAGGACT CTATGTTACT ACCACAAAAG ATGCACTGGA AACCAACATA

601 AGTTGGGCTA ATGCTATGAC ATTTATAGGA AATGCCATGG GTGTCAATAT TGATACACAA

661 AAAGGCTTGC AATTTGGCAC CACTAGTACC GTCGCAGATG TTAAAAACGC TTACCCCATA

721 CAAGTCAAAC TGGGAGCTGG TCTCACATTT GACAGCACAG GTGCAATTGT CGCTTGGAAC

781 AAAGAAGATG ACAAACTTAC ACTGTGGACC ACAGCCGATC CATCTCCAAA CTGTCACATA

841 TATTCTGACA AGGATGCTAA GCTTACACTC TGCTTGACAA AGTGTGGCAG TCAGATACTG

901 GGCACTGTTT CTCTCATAGC TGTTGATACT GGTAGCTTAA ATCCAATAAC AGGACAAGTA

961 ACCACTGCTC TTGTTTCACT TAAATTCGAT GCCAATGGAG TTTTGCAAAC CAGTTCAACA

1021 TTGGACAAAG AATATTGGAA TTTTAGAAAA GGAGATGTGA CACCTGCTGA GCCATATACT

1081 AATGCTATAG GTTTCATGCC CAATCTAAAG GCATACCCTA AAAACACAAG TGGAGCTGCA

Fig. 13A

1141 AAAAGTCACA TTGTTGGGAA AGTGTACCTA CATGGGGATA CAGACAAACC
ACTGGACCTG

1201 ATTATTACTT TCAATGAAAC AAGTGATGAA TCTTGCACTT ACTGTATTAA
CTTTCAATGG

1261 AAATGGGATA GTACTAAGTA CACAGGTGAA ACACTTGCTA CAAGCTCCTT
CACCTTCTCC

1321 TACATTGCCC AAGAATGA

Fig. 13B

1 ATGTCCAAAA AGCGCGTCCG GGTGGATGAT GACTTCGACC CCGTCTACCC CTACGATGCA

61 GACAACGCAC CGACCGTGCC CTTCATCAAC CCCCCCTTCG TCTCTTCAGA TGGATTCCAA

121 GAGAAGCCCC TGGGGGTGTT GTCCCTGCGA CTGGCCGACC CCGTCACCAC CAAGAACGGG

181 GAAATCACCC TCAAGCTGGG AGAGGGGGTG GACCTCGACT CCTCGGGAAA ACTCATCTCC

241 AACACGGCCA CCAAGGCCGC TGCCCCTCTC AGTTTTTCCA ACAACACCAT TTCCCTTAAC

301 ATGGATCACC CCTTTTACAC TAAAGATGGA AAATTAGCCT TACAAGTTTC TCCACCATTA

361 AATATACTGA GAACAAGCAT TCTAAACACA CTAGCTTTAG GTTTTGGATC AGGTTTAGGA

421 CTCCGTGGCT CTGCCTTGGC AGTACAGTTA GTCTCTCCAC TTACATTTGA TACTGATGGA

481 AACATAAAGC TTACCTTAGA CAGAGGTTTG CATGTTACAA CAGGAGATGC AATTGAAAGC

541 AACATAAGCT GGGCTAAAGG TTTAAAATTT GAAGATGGAG CCATAGCAAC CAACATTGGA

601 AATGGGTTAG AGTTTGGAAG CAGTAGTACA GAAACAGGTG TCGATGATGC TTACCCAATC

661 CAAGTTAAAC TTGGATCTGG CCTTAGCTTT GACAGTACAG GAGCCATAAT GGCTGGTAAC

721 AAAGAAGACG ATAAACTCAC TTTGTGGACA ACACCTGATC CATCACCAAA CTGTCAAATA

781 CTCGCAGAAA ATGATGCAAA ACTAACACTT TGCTTGACTA AATGTGGTAG TCAAATACTG

841 GCCACTGTGT CAGTCTTAGT TGTAGGAAGT GGAGACCTAA ACCCCATTAC TGGCACCGTA

901 AGCAGTGCTC AGGTGTTTCT ACGTTTTGAT GCAAACGGTG TTCTTTTAAC AGAACATTCT

961 ACACTAAAAA AATACTGGGG GTATAGGCAG GGAGATAGCA TAGATGGCAC TCCATATGCC

1021 AATGCTGTAG GATTCATGCC CAATTTAAAA GCTTATCCAA AGTCACAAAG TTCTACTACT

1081 AAAAATAATA TAGTAGGGCA AGTATACATG AATGGAGATG TTTCAAAACC TATGCTTCTC

1141 ACTATAACCC TCAATGGTAC TGATGACAGC AACAGTACAT ATTCAATGTC ATTTTCATAC

Fig. 14A

1201 ACCTGGACTA ATGGAAGCTA TGTTGGAGCA ACATTTGGAG CTAACTCTTA TACCTTCTCC

1261 TACATCGCCC AAGAATGA

Fig. 14B

```
        1  ATGTCCAAAA AGCGCGTCCG GGTGGATGAT GACTTCGACC CCGTCTACCC
CTACGATGCA

       61  GACAACGCAC CGACCGTGCC CTTCATCAAC CCCCCCTTCG TCTCTTCAGA
TGGATTCCAA

      121  GAGAAGCCCC TGGGGGTGCT GTCCCTGCGA CTGGCCGACC CCGTCACCAC
CAAGAACGGG

      181  GAAATCACCC TCAAGCTGGG AGAGGGGGTG GACCTCGACT CCTCGGGAAA
ACTCATCTCC

      241  AACACGGCCA CCAAGGCCGC CGCCCCTCTC AGTTTTTCCA ACAACACCAT
TTCCCTTAAC

      301  ATGGATCACC CCTTTTACAC TAAAGATGGA AAATTATCCT TACAAGTTTC
TCCACCATTA

      361  AATATACTGA GAACAAGCAT TCTAAACACA CTAGCTTTAG GTTTTGGATC
AGGTTTAGGA

      421  CTCCGTGGCT CTGCCTTGGC AGTACAGTTA GTCTCTCCAC TTACATTTGA
TACTGATGGA

      481  AACATAAAGC TTACCTTAGA CAGAGGTTTG CATGTTACAA CAGGAGATGC
AATTGAAAGC

      541  AACATAAGCT GGGCTAAAGG TTTAAAATTT GAAGATGGAG CCATAGCAAC
CAACATTGGA

      601  AATGGGTTAG AGTTTGGAAG CAGTAGTACA GAAACAGGTG TTGATGATGC
TTACCCAATC

      661  CAAGTTAAAC TTGGATCTGG CCTTAGCTTT GACAGTACAG GAGCCATAAT
GGCTGGTAAC

      721  AAAGAAGACG ATAAACTCAC TTTGTGGACA ACACCTGATC CATCGCCAAA
CTGTCAAATA

      781  CTCGCAGAAA ATGATGCAAA ACTAACACTT TGCTTGACTA AATGTGGTAG
TCAAATACTG

      841  GCCACTGTGT CAGTCTTAGT TGTAGGAAGT GGAAACCTAA ACCCCATTAC
TGGCACCGTA

      901  AGCAGTGCTC AGGTGTTTCT ACGTTTTGAT GCAAACGGTG TTCTTTTAAC
AGAACATTCT

      961  ACACTAAAAA AATACTGGGG GTATAGGCAG GGAGATAGCA TAGATGGCAC
TCCATATACC

     1021  AATGCTGTAG GATTCATGCC CAATTTAAAA GCTTATCCAA AGTCACAAAG
TTCTACTACT

     1081  AAAAATAATA TAGTAGGGCA AGTATACATG AATGGAGATG TTTCAAAACC
TATGCTTCTC
```

Fig. 15A

1141 ACTATAACCC TCAATGGTAC TGATGACAGC AACAGTACAT ATTCAATGTC ATTTTCATAC

1201 ACCTGGACTA ATGGAAGCTA TGTTGGAGCA ACATTTGGGG CTAACTCTTA TACCTTCTCA

1261 TACATCGCCC AAGAATGA

Fig. 15B

```
        1  ATGAAGCGCA CCAAAACGTC TGACGAGAGC TTCAACCCCG TGTACCCCTA
TGACACGGAA

       61  AACGGTCCTC CCTCCGTCCC TTTCCTCACC CCTCCCTTCG TGTCTCCCGA
TGGATTCCAA

      121  GAGAGCCCCC CCGGGGTCCT GTCTCTGAAC CTGGCCGAGC CCCTGGTCAC
TTCCCACGGC

      181  ATGCTCGCCC TGAAAATGGG AAGTGGCCTC TCCCTGGACG ACGCCGGCAA
CCTCACCTCT

      241  CAAGATGTCA CCACCACTAC CCCTCCCCTG AAAAAAACCA AGACCAACCT
CAGCCTAGAA

      301  ACCTCAGCCC CCCTGACTGT GAGCACCTCA GGCGCCCTCA CCCTAGCAGC
CGCCGTTCCC

      361  CTGGCGGTGG CCGGCACCTC CCTCACCATG CAÀTCAGAGG CCCCCCTGAC
AGTCCAAGAT

      421  GCAAAACTCA CCCTGGCCAC CAAGGGCCCC CTGACCGTGT CTGAAGGCAA
ACTAGCCTTG

      481  CAGACCTCGG CCCCGCTGAC GGCCGCTGAC AGCAGCACCC TCACAATCAG
CGCCACACCG

      541  CCCCTTAGCA CAAGCAATGG CAGCTTGGGT ATTGACATGC AAGCCCCCAT
TTACACTACT

      601  AACGGAAAAC TGGGACTTAA CTTTGGTGCT CCCCTGCATG TGGTAGACAG
CCTAAATGCA

      661  CTGACTGTAG TGACTGGCCA AGGTCTTACG ATAAACGGTA CAGCCCTACA
AACTAGAGTC

      721  TCAGGTGCCC TCAACTATGA CTCATCAGGA AACCTAGAAT TGAGAGCTGC
AGGGGGTATG

      781  CGAGTTGATG CAAATGGCAA ACTTATCCTT GACGTAGCTT ACCCATTTGA
TGCTCAAAAC

      841  AACCTCAGCC TTAGACTTGG ACAGGGACCC CTGTTTGTTA ACTCTGCCCA
CAACTTGGAT

      901  GTTAACTACA ACAGAGGCCT CTACCTGTTC ACATCTGGAA ATACCAAAAA
GCTAGAAGTT

      961  AATATCAAAA CAGCCAAAGG CCTCATTTAT GATGACACTG CTATAGCAAT
CAATCCAGGC

     1021  GATGGGCTAG AGTTTGGCTC AGGCTCAGAT ACAAATCCAT TAAAAACTAA
ACTTGGATTG

     1081  GGACTAGAGT ATGACTCCAG CAGAGCCATA ATTGCTAAGC TGGGAACCGG
CCTAAGCTTT
```

Fig. 16A

1141 GACAACACAG GTGCCATCAC AGTGGGCAAC AAAAATGATG ACAAGCTTAC CTTGTGGACC

1201 ACACCAGACC CCTCTCCCAA CTGTAGAATT TATTCAGAAA AAGATGCTAA ATTTACACTA

1261 GTTTTAACTA AATGCGGCAG TCAGGTGTTG GCCAGCGTTT CTGTTTTATC TGTAAAAGGC

1321 AGCCTTGCGC CCATCAGTGG CACAGTAACT AGCGCTCAGA TTATTCTCAG ATTTGATGAA

1381 AATGGAGTTC TACTAAGCAA TTCTTCTCTT GACCCCCAAT ACTGGAACTA CAGAAAAGGT

1441 GACCTTACAG AGGGCACTGC ATATACCAAC GCAGTGGGAT TTATGCCCAA CCTCACAGCA

1501 TACCCAAAAA CACAGAGTCA AACTGCTAAA AGCAACATTG TAAGCCAGGT TTACTTGAAT

1561 GGGGACAAAT CCAAACCCAT GATCCTCACC ATTACCCTCA ATGGAACTAA TGAAACAGGG

1621 GATGCTACAG TTAGCACTTA CTCCATGTCA TTCTCATGGA ATTGGAATGG AAGTAATTAC

1681 ATTAATGAAA CGTTCCAAAC CAACTCTTTC ACCTTCTCCT ACATCGCCCA AGAATAA

Fig. 16B

```
        1  ATGTCCAAAA AGCGCGTCCG GGTGGATGAT GACTTCGACC CCGTCTACCC
CTACGATGCA

       61  GACAACGCAC CGACCGTGCC CTTCATCAAC CCCCCCTTCG TCTCTTCAGA
TGGATTCCAA

      121  GAGAAGCCCC TGGGGGTGCT GTCCCTGCGA CTGGCTGACC CCGTCACCAC
CAAGAACGGG

      181  GAAATCACCC TCAAGCTGGG AGAGGGGGTG GACCTCGACT CCTCGGGAAA
ACTCATCTCC

      241  AACACGGCCA CCAAGGCCGC CGCCCCTCTC AGTTTTTCCA ACAACACCAT
TTCCCTTAAC

      301  ATGGATACCC CTTTTTACAC CAAAGATGGA AAATTAACCA TGCAGGTCAC
TGCACCACTA

      361  AAGTTAGCAA ACACAGCCAT ATTGAACACA CTAGCTATGG CATATGGAAA
TGGATTAGGT

      421  CTAAGCAACA ACGCTCTTAC CGTTCAGTTA CAATCTCCAC TCACCTTTAA
CAACAGCAAG

      481  GTTGCAATCA ACCTGGGAAA TGGACCACTA AATGTAACAT CAAACAGACT
TAGCATTAAT

      541  TGCAAGAGGG GTGTCTATGT CACCACCACA GGAGATGCAA TTGAAACCAA
CATAAGTTGG

      601  TCAAATGCTA TTAAATTTAT AGGAAATGCC ATGGGTGTCA ACATTGATAC
AAACAAAGGC

      661  TTGCAATTTG GCACCACCAG CACTGTCACA GATGTGACCA ATGCTTTCCC
CATACAAGTC

      721  AAACTTGGGG CTGGTCTTGC ATTTGATAGC ACTGGAGCTA TTGTTGCATG
GAACAAAGAG

      781  GATGACAGTC TCACTTTGTG GACTACACCA GATCCATCTC CAAATTGCAA
GATAGCATCT

      841  GACAAAGATG CTAAACTCAC ACTTTGCTTG ACAAAATGTG GTAGTCAGAT
ACTGGGCACT

      901  GTCTCCTTGT TAGCTGTGAG TGGCAGTTTA GCTCCTATCA CTGGAGCTGT
GAGCACTGCA

      961  CTTGTATCAC TTAAATTCGA TGCCAATGGA GCACTCTTGG AAAAATCAAC
CCTAAACAGA

     1021  GAATATTGGA ACTATAGACA AGGAGATCTT ATTCCAGGTA CGCCATATAC
TCACGCAGTA

     1081  GGTTTCATGC CCAACAAGAA AGCCTACCCT AAAAACACAA CTGCAGCTTC
CAAAAGCCAC
```

Fig. 17A

1141 ATTGTGGGAG AAGTCTATCT AGACGGAGAT GCAGATAAGC CCCTATCTCT CATAATCACT

1201 TTTAATGAAA CTGATGATGA ATCATGTGAC TATTGCATGA ACTTTCAATG GAAATGGGGT

1261 GCTGATCAAT ACAAGGACAA AACACTCGCT ACCAGCTCCT TCACCTTCTC CTACATTGCC

1321 CAAGAATGA

Fig. 17B

```
       1  ATGAAGCGCA CCAAAACGTC TGACGAGAGC TTCAACCCCG TGTACCCCTA
TGACACGGAA

      61  AGCGGCCCTC CCTCCGTCCC TTTCCTCACC CCTCCCTTCG TGTCTCCCGA
TGGATTCCAA

     121  GAAAGCCCCC CCGGGGTCCT GTCTCTGAAC CTGGCCGAGC CCCTGGTCAC
TTCCCACGGC

     181  ATGCTTGCCC TGAAAATGGG AAGTGGCCTC TCCCTGGACG ACGCTGGCAA
CCTTACCTCT

     241  CAAGATATTA CCTCCACTAC CCCTCCCCTC AAAAAAACCA AGACCAACCT
CAGCCTAGAA

     301  ACCTCATCCC CCCTAACTGT AAGCACCTCA GGCGCCCTCA CCGTAGCAGC
CGCCGCTCCC

     361  CTGGCGGTGG CCGGCACCTC CCTCACCATG CAATCAGAGG CCCCCCTGGC
AGTACAGGAT

     421  GCAAAACTCA CCCTGGCCAC CAAAGGCCCC CTGACCGTGT CTGAAGGCAA
ACTGGCCTTG

     481  CAAACATCGG CCCCGCTGAC GGCCGCTGAC AGCAGCACCC TCACCGTTAG
CTCCACTCCA

     541  CCAATTAGTG TAAGCAGTGG AAGTTTGGGC TTGGACATGG AAGACCCCAT
GTATACTCAC

     601  GATGGAAAAC TGGGAATAAG AATTGGGGGT CCACTAAGAG TAGTAGACAG
CTTGCACACA

     661  CTCACTGTAG TTACCGGAAA TGGACTAACT GTAGATAACA ATGCCCTCCA
AACTAGAGTT

     721  ACGGGCGCCC TAGGTTATGA CACATCAGGA AATCTACAAC TGAGAGCCGC
AGGGGGTATG

     781  CGAATTGATG CAAATGGCCA ACTTATCCTT GATGTGGCAT ACCCATTTGA
TGCTCAAAAC

     841  AATCTCAGCC TTAGACTTGG TCAGGGACCC CTGTATGTAA ATACAGACCA
CAACCTGGAT

     901  TTAAATTGCA ACAGAGGTCT AACCACAACT ACCACCAACA ACACAAAAAA
ACTTGAGACT

     961  AAAATTAGCT CAGGCTTAGA CTATGACACC AATGGTGCTG TCATTATTAA
ACTTGGCACT

    1021  GGTCTAAGCT TCGACAACAC AGGCGCCCTA ACTGTGGGAA ACACTGGTGA
TGATAAACTG

    1081  ACTCTGTGGA CGACCCCAGA CCCATCTCCA AATTGCAGAA TTCACTCAGA
CAAAGACTGC
```

Fig. 18A

1141 AAGTTTACTC TCGTCCTAAC TAAGTGTGGA AGCCAAATCC TGGCCTCTGT CGCCGCCCTA

1201 GCGGTATCAG GAAATCTGGC TTCGATAACA GGCACCGTTG CCAGCGTTAC CATCTTTCTT

1261 AGATTTGATC AGAATGGAGT GCTTATGGAA AACTCCTCAC TAGACAAGCA GTACTGGAAC

1321 TTCAGAAATG GCAATTCAAC TAATGCTGCC CCCTACACCA ACGCAGTTGG GTTCATGCCA

1381 AACCTCGCAG CGTACCCCAA AACGCAAAGC CAGACTGCTA AAAACAACAT TGTAAGTCAG

1441 GTTTACTTGA ATGGAGACAA ATCCAAACCC ATGACCCTTA CCATCACCCT CAATGGAACT

1501 AATGAATCCA GTGAAACTAG TCAGGTGAGT CACTACTCCA TGTCATTTAC ATGGGCTTGG

1561 GAAAGCGGGC AATATGCCAC TGAAACCTTT GCCACCAACT CCTTCACCTT TTCTTACATT

1621 GCTGAACAAT AA

Fig. 18B

```
      1  ATGAAGCGCA CCAAAACGTC TGACAAGAGC TTCAACCCCG TGTACCCCTA
TGACACGGAA

     61  AACGGTCCTC CCTCCGTCCC TTTCCTCACC CCTCCCTTCG TGTCTCCCGA
TGGATTCCAA

    121  GAGAGCCCCC CCGGGGTCCT GTCTCTGAAC CTGGCCGAGC CCCTGGTCAC
TTCCCACGGC

    181  ATGCTCGCCC TGAAAATGGG AAGTGGCCTC TCCCTGGACG ACGCCGGCAA
CCTCACCTCT

    241  CAAGATGTCA CCACCACTAC CCCTCCCCTG AAAAAAACCA AGACCAACCT
CAGCCTAGAA

    301  ACCTCAGCCC CCCTGACTGT GAGCACCTCA GGCGCCCTCA CCCTAGCAGC
CGCCGCCCCC

    361  CTGGCGGTGG CCGGCACCTC CCTCACCATG CAATCAGAGG CCCCCCTGAC
AGTCCAAGAT

    421  GCAAAACTCA CCCTGGCCAC CAAGGGCCCC CTGACCGTGT CTGAAGGCAA
ACTGGCCTTG

    481  CAGACCTCGG CCCCGCTGAC GGCCGCTGAC AGCAGCACCC TCACCGTTAG
CGCCACACCA

    541  CCCATCAGTG TAAGCAGTGG AAGTTTGGGC TTAGACATGG AAGACCCAAT
GTATACTCAT

    601  GATGGAAAAC TGGGAATAAG AATTGGGGGC CCACTGAGAG TAGTAGACAG
CCTGCACACA

    661  CTGACTGTAG TTACCGGAAA TGGAATAGCT GTAGATAACA ATGCCCTCCA
AACTAGAGTT

    721  ACGGGCGCCC TGGGTTATGA CACATCAGGA AACCTACAAC TGAGAGCCGC
GGGGGGTATG

    781  CGAATTGATG CAAATGGCCA ACTTATCCTT GATGTGGCAT ACCCATTTGA
TGCTCAAAAC

    841  AATCTCAGCC TTAGACTTGG TCAGGGACCC CTGTATGTAA ACACAGACCA
CAACCTAGAT

    901  TTGAATTGCA ACAGAGGTCT GACCACAACT ACCACCAACA ACACAAAAAA
ACTTGAAACT

    961  AAAATTGGCT CAGGCTTAGA CTATGATACC AATGGTGCTG TTATTATTAA
ACTTGGCACT

   1021  GGTGTCAGCT TTGACAGCAC AGGTGCCCTA AGTGTGGGAA ACACTGGCGA
TGATAAACTG

   1081  ACTCTGTGGA CAACCCCAGA CCCATCTCCA AATTGCAGAA TTCACTCAGA
CAAAGACTGC
```

Fig. 19A

1141 AAGTTTACTC TAGTCCTAAC TAAGTGTGGA AGTCAAATCC TGGCTTCTGT CGCCGCCCTA

1201 GCGGTGTCAG GAAATCTGGC TTCAATAACA GGCACCGTTT CCAGCGTTAC CATCTTTCTC

1261 AGATTTGATC AGAATGGAGT GCTTATGGAA AACTCCTCGC TAGACAAGCA GTACTGGAAC

1321 TTCAGAAATG GTAATTCAAC CAATGCCACC CCCTACACCA ATGCAGTTGG GTTTATGCCA

1381 AACCTCGCAG CATACCCCAA GACACAGAGC CAGACTGCAA AAAACAACAT TGTAAGTCAG

1441 GTTTACTTGA ATGGGGACAA ATCCAAACCC ATGACCCTTA CCATTACCCT CAATGGAACT

1501 AATGAATCCA GTGAAACTAG CCAGGTGAGT CACTACTCCA TGTCATTTAC GTGGGCTTGG

1561 GAGAGTGGGC AATATGCCAC CGAAACCTTT GCCACCAATT CCTTTACCTT CTCTTACATT

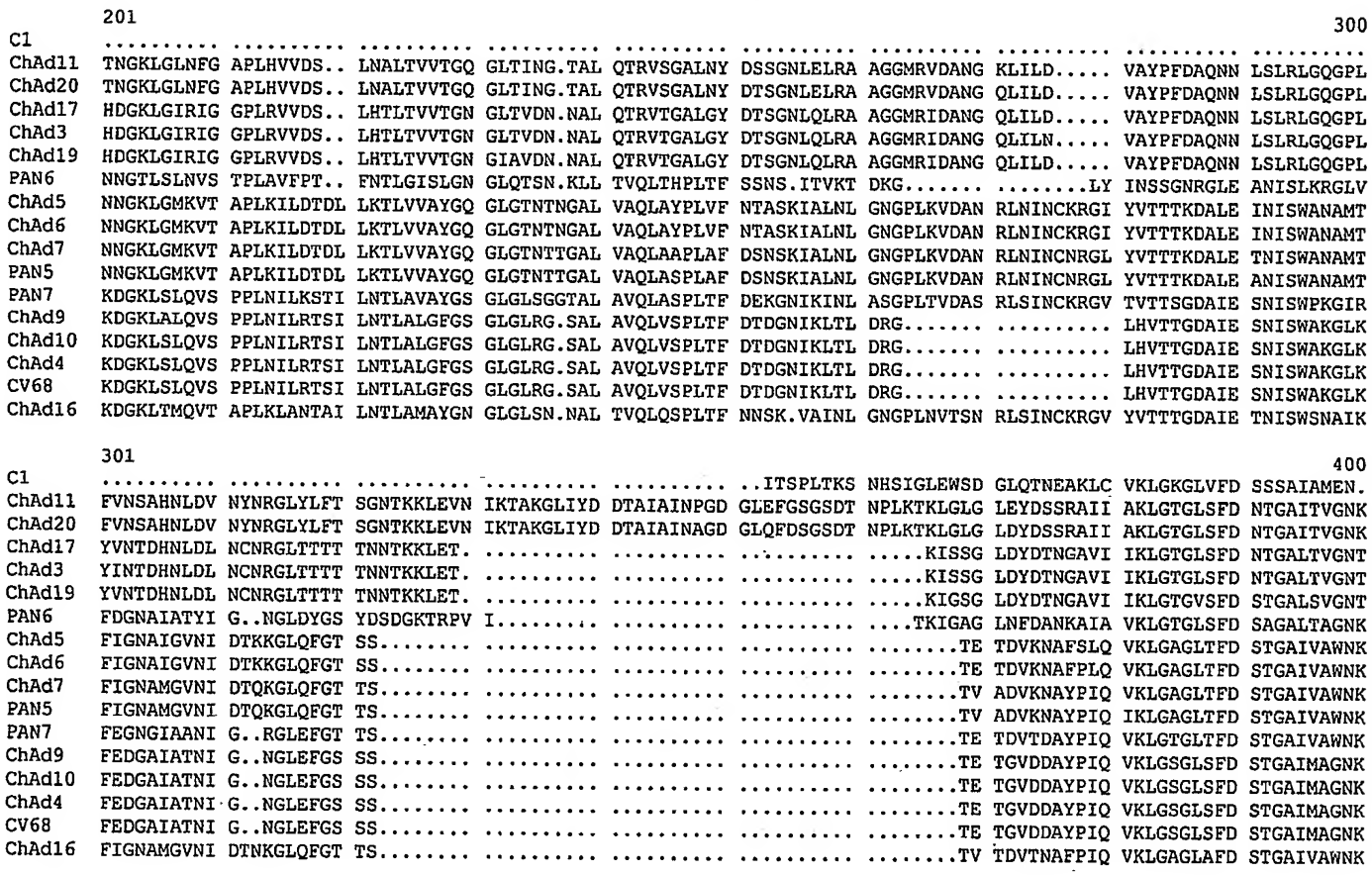
1621 GCTGAACAAT AA

Fig. 19B

```
        1                                                                                                              100
C1      MAKRTRLSSS .FNPVYPYED EN..SSHPFI NPGFISPNGF TQSPDGVLTL NCVAPLTTAN GALDIKVGGG LKVNSTDGFL EENIN..... ..........
ChAd11  MKRTKTSDES .FNPVYPYDT ENGPPSVPFL TPPFVSPDGF QESPPGVLSL NLAEPLVTSH GMLALKMGSG LSLDDAGNLT SQDVTTTTPP LKKTKTNLSL
ChAd20  MKRTKTSDES .FNPVYPYDT ESGPPSVPFL TPPFVSPDGF QESPPGVLSL NLAEPLVTSH GMLALKMGSG LSLDDAGNLT SQDITTASPP LKKTKTNLSL
ChAd17  MKRTKTSDES .FNPVYPYDT ESGPPSVPFL TPPFVSPDGF QESPPGVLSL NLAEPLVTSH GMLALKMGSG LSLDDAGNLT SQDITSTTPP LKKTKTNLSL
ChAd3   MKRTKTSDES .FNPVYPYDT ESGPPSVPFL TPPFVSPDGF QESPPGVLSL NLAEPLVTSH GMLALKMGSG LSLDDAGNLT SQDITTASPP LKKTKTNLSL
ChAd19  MKRTKTSDKS .FNPVYPYDT ENGPPSVPFL TPPFVSPDGF QESPPGVLSL NLAEPLVTSH GMLALKMGSG LSLDDAGNLT SQDVTTTTPP LKKTKTNLSL
PAN6    MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGEG VDLDSSGKLI SNTAT..... ..........
ChAd5   MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGDG VDLDDSGKLI SNTAT..... ..........
ChAd6   MSKKRARVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GAVTLKLGEG VDLDDSGKLI SKNAT..... ..........
ChAd7   MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGEG VDLDSSGKLI SNTAT..... ..........
PAN5    MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGDG VDLDSSGKLI SNTAT..... ..........
PAN7    MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGEG VDLDSSGKLI SNTAT..... ..........
ChAd9   MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGEG VDLDSSGKLI SNTAT..... ..........
ChAd10  MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGEG VDLDSSGKLI SNTAT..... ..........
ChAd4   MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGEG VDLDSSGKLI SNTAT..... ..........
CV68    MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGEG VDLDSSGKLI SNTAT..... ..........
ChAd16  MSKKRVRVDD DFDPVYPYDA DN.APTVPFI NPPFVSSDGF QEKPLGVLSL RLADPVTTKN GEITLKLGEG VDLDSSGKLI SNTAT..... ..........

        101                                                                                                            200
C1      .......... .......... .......... .......... .......... .......... .......... .......... .......... ..........
ChAd11  ETSAPLTVST SGALTLAAAV PLAVAGTSLT MQSEAPLTVQ DAKLTLATKG PLTVSEGKLA LQTSAPLTAA DSSTLTISAT PPLSTSNGSL GIDMQAPIYT
ChAd20  ETSSPLTVST SGALTVAAAA PLAVAGTSLT MQSEAPLTVQ DAKLTLATKG PLTVSEGKLA LQTSAPLTAA DSSTLTVSAT PPLSTSNGSL GIDMQAPIYT
ChAd17  ETSSPLTVST SGALTVAAAA PLAVAGTSLT MQSEAPLAVQ DAKLTLATKG PLTVSEGKLA LQTSAPLTAA DSSTLTVSST PPISVSSGSL GLDMEDPMYT
ChAd3   ETSSPLTVST SGALTVAAAA PLAVAGTSLT MQSEAPLTVQ DAKLTLATKG PLTVSEGKLA LQTSAPLTAA DSSTLTVSAT PPINVSSGSL GLDMEDPMYT
ChAd19  ETSAPLTVST SGALTLAAAA PLAVAGTSLT MQSEAPLTVQ DAKLTLATKG PLTVSEGKLA LQTSAPLTAA DSSTLTVSAT PPISVSSGSL GLDMEDPMYT
PAN6    .......... .......... .......... .......... .......... .......... .......... .......KAA APLSISNNTI SLKTAAPFYN
ChAd5   .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDTPLYN
ChAd6   .......... .......... .......... .......... .......... .......... .......... .......KAT APLSISNNTI SLNMDTPLYN
ChAd7   .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDTPFYN
PAN5    .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDTPFYN
PAN7    .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDTPLYT
ChAd9   .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDHPFYT
ChAd10  .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDHPFYT
ChAd4   .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDHPFYT
CV68    .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDHPFYT
ChAd16  .......... .......... .......... .......... .......... .......... .......... .......KAA APLSFSNNTI SLNMDTPFYT
```

Fig. 20A



```
          201                                                                                                  300
C1        .......... .......... .......... .......... .......... .......... .......... .......... .......... ..........
ChAd11    TNGKLGLNFG APLHVVDS.. LNALTVVTGQ GLTING.TAL QTRVSGALNY DSSGNLELRA AGGMRVDANG KLILD..... VAYPFDAQNN LSLRLGQGPL
ChAd20    TNGKLGLNFG APLHVVDS.. LNALTVVTGQ GLTING.TAL QTRVSGALNY DTSGNLELRA AGGMRVDANG QLILD..... VAYPFDAQNN LSLRLGQGPL
ChAd17    HDGKLGIRIG GPLRVVDS.. LHTLTVVTGN GLTVDN.NAL QTRVTGALGY DTSGNLQLRA AGGMRIDANG QLILD..... VAYPFDAQNN LSLRLGQGPL
ChAd3     HDGKLGIRIG GPLRVVDS.. LHTLTVVTGN GLTVDN.NAL QTRVTGALGY DTSGNLQLRA AGGMRIDANG QLILN..... VAYPFDAQNN LSLRLGQGPL
ChAd19    HDGKLGIRIG GPLRVVDS.. LHTLTVVTGN GIAVDN.NAL QTRVTGALGY DTSGNLQLRA AGGMRIDANG QLILD..... VAYPFDAQNN LSLRLGQGPL
PAN6      NNGTLSLNVS TPLAVFPT.. FNTLGISLGN GLQTSN.KLL TVQLTHPLTF SSNS.ITVKT DKG..... .....LY INSSGNRGLE ANISLKRGLV
ChAd5     NNGKLGMKVT APLKILDTDL LKTLVVAYGQ GLGTNTNGAL VAQLAYPLVF NTASKIALNL GNGPLKVDAN RLNINCKRGI YVTTTKDALE INISWANAMT
ChAd6     NNGKLGMKVT APLKILDTDL LKTLVVAYGQ GLGTNTNGAL VAQLAYPLVF NTASKIALNL GNGPLKVDAN RLNINCKRGI YVTTTKDALE INISWANAMT
ChAd7     NNGKLGMKVT APLKILDTDL LKTLVVAYGQ GLGTNTTGAL VAQLAAPLAF DSNSKIALNL GNGPLKVDAN RLNINCNRGL YVTTTKDALE TNISWANAMT
PAN5      NNGKLGMKVT APLKILDTDL LKTLVVAYGQ GLGTNTTGAL VAQLASPLAF DSNSKIALNL GNGPLKVDAN RLNINCNRGL YVTTTKDALE ANISWANAMT
PAN7      KDGKLSLQVS PPLNILKSTI LNTLAVAYGS GLGLSGGTAL AVQLASPLTF DEKGNIKINL ASGPLTVDAS RLSINCKRGV TVTTSGDAIE SNISWPKGIR
ChAd9     KDGKLALQVS PPLNILRTSI LNTLALGFGS GLGLRG.SAL AVQLVSPLTF DTDGNIKLTL DRG..... ..... LHVTTGDAIE SNISWAKGLK
ChAd10    KDGKLSLQVS PPLNILRTSI LNTLALGFGS GLGLRG.SAL AVQLVSPLTF DTDGNIKLTL DRG..... ..... LHVTTGDAIE SNISWAKGLK
ChAd4     KDGKLSLQVS PPLNILRTSI LNTLALGFGS GLGLRG.SAL AVQLVSPLTF DTDGNIKLTL DRG..... ..... LHVTTGDAIE SNISWAKGLK
CV68      KDGKLSLQVS PPLNILRTSI LNTLALGFGS GLGLRG.SAL AVQLVSPLTF DTDGNIKLTL DRG..... ..... LHVTTGDAIE SNISWAKGLK
ChAd16    KDGKLTMQVT APLKLANTAI LNTLAMAYGN GLGLSN.NAL TVQLQSPLTF NNSK.VAINL GNGPLNVTSN RLSINCKRGV YVTTTGDAIE TNISWSNAIK

          301                                                                                                  400
C1        .......... .......... .......... .......... .......... ..ITSPLTKS NHSIGLEWSD GLQTNEAKLC VKLGKGLVFD SSSAIAMEN.
ChAd11    FVNSAHNLDV NYNRGLYLFT SGNTKKLEVN IKTAKGLIYD DTAIAINPGD GLEFGSGSDT NPLKTKLGLG LEYDSSRAII AKLGTGLSFD NTGAITVGNK
ChAd20    FVNSAHNLDV NYNRGLYLFT SGNTKKLEVN IKTAKGLIYD DTAIAINAGD GLQFDSGSDT NPLKTKLGLG LDYDSSRAII AKLGTGLSFD NTGAITVGNK
ChAd17    YVNTDHNLDL NCNRGLTTTT TNNTKKLET. .......... .......... .......... .....KISSG LDYDTNGAVI IKLGTGLSFD NTGALTVGNT
ChAd3     YINTDHNLDL NCNRGLTTTT TNNTKKLET. .......... .......... .......... .....KISSG LDYDTNGAVI IKLGTGLSFD NTGALTVGNT
ChAd19    YVNTDHNLDL NCNRGLTTTT TNNTKKLET. .......... .......... .......... .....KIGSG LDYDTNGAVI IKLGTGVSFD STGALSVGNT
PAN6      FDGNAIATYI G..NGLDYGS YDSDGKTRPV I.......... .......... .......... ....TKIGAG LNFDANKAIA VKLGTGLSFD SAGALTAGNK
ChAd5     FIGNAIGVNI DTKKGLQFGT SS........ .......... .......... .......... ........TE TDVKNAFSLQ VKLGAGLTFD STGAIVAWNK
ChAd6     FIGNAIGVNI DTKKGLQFGT SS........ .......... .......... .......... ........TE TDVKNAFPLQ VKLGAGLTFD STGAIVAWNK
ChAd7     FIGNAMGVNI DTQKGLQFGT TS........ .......... .......... .......... ........TV ADVKNAYPIQ VKLGAGLTFD STGAIVAWNK
PAN5      FIGNAMGVNI DTQKGLQFGT TS........ .......... .......... .......... ........TV ADVKNAYPIQ IKLGAGLTFD STGAIVAWNK
PAN7      FEGNGIAANI G..RGLEFGT TS........ .......... .......... .......... ........TE TDVTDAYPIQ VKLGTGLTFD STGAIVAWNK
ChAd9     FEDGAIATNI G..NGLEFGS SS........ .......... .......... .......... ........TE TGVDDAYPIQ VKLGSGLSFD STGAIMAGNK
ChAd10    FEDGAIATNI G..NGLEFGS SS........ .......... .......... .......... ........TE TGVDDAYPIQ VKLGSGLSFD STGAIMAGNK
ChAd4     FEDGAIATNI G..NGLEFGS SS........ .......... .......... .......... ........TE TGVDDAYPIQ VKLGSGLSFD STGAIMAGNK
CV68      FEDGAIATNI G..NGLEFGS SS........ .......... .......... .......... ........TE TGVDDAYPIQ VKLGSGLSFD STGAIMAGNK
ChAd16    FIGNAMGVNI DTNKGLQFGT TS........ .......... .......... .......... ........TV TDVTNAFPIQ VKLGAGLAFD STGAIVAWNK
```

Fig. 20B

```
         401                                                                                                              500
C1       ....NTLWTG AKPSANCVIK EGEDSPDCKL TLVLVKNGGL VNGYITLMGD SE.YTNTLFK NKQVTIDVNL AFDNTGQIIT YLSSLKS.NL NFKDNQNMAT
ChAd11   NDDKLTLWTT PDPSPNCRIY SE...KDAKF TLVLTKCGSQ VLASVSVLSV K..GSLAPIS GTVTSAQIIL RFDENGVLLS N.SSLDPQYW NYRK.GDLTE
ChAd20   NDDKLTLWTT PDPSPNCRIY SE...KDAKF TLVLTKCGSQ VLASVSVLSV K..GSLAPIS GTVTSAQIVL RFDENGVLLS N.SSLDPQYW NYRK.GDLTE
ChAd17   GDDKLTLWTT PDPSPNCRIH SD...KDCKF TLVLTKCGSQ ILASVAALAV S..GNLASIT GTVASVTIFL RFDQNGVLME N.SSLDKQYW NFRN.GNSTN
ChAd3    GDDKLTLWTT PDPSPNCRIH SD...KDCKF TLVLTKCGSQ ILASVAALAV S..GNLASIT GTVASVTIFL RFDQNGVLME N.SSLDRQYW NFRN.GNSTN
ChAd19   GDDKLTLWTT PDPSPNCRIH SD...KDCKF TLVLTKCGSQ ILASVAALAV S..GNLASIT GTVSSVTIFL RFDQNGVLME N.SSLDKQYW NFRN.GNSTN
PAN6     QDDKLTLWTT PDPSPNCQLL SD...RDAKF TLCLTKCGSQ ILGTVAVAAV TVGSALNPIN DTVKSAIVFL RFDSDGVLMS N.SSMVGDYW NFRE.GQTTQ
ChAd5    EDDKLTLWTT ADPSPNCHIY SA...KDAKL TLCLTKCGSQ ILGTVSLLAV S..GSLAPIT GAVRTALVSL KFNANGALLD K.STLNKEYW NYRQ.GDLIP
ChAd6    EDDKLTLWTT ADPSPNCHIY SA...KDAKL TLCLTKCGSQ ILGTVSLIAV DT.GSLNPIT GKVTTALVSL KFDANGVLQA S.STLDKEYW NFRK.GDVTP
ChAd7    EDDKLTLWTT ADPSPNCHIY SD...KDAKL TLCLTKCGSQ ILGTVSLIAV DT.GSLNPIT GQVTTALVSL KFDANGVLQT S.STLDKEYW NFRK.GDVTP
PAN5     DDDKLTLWTT ADPSPNCHIY SE...KDAKL TLCLTKCGSQ ILGTVSLIAV DT.GSLNPIT GTVTTALVSL KFDANGVLQS S.STLDSDYW NFRQ.GDVTP
PAN7     EDDKLTLWTT ADPSPNCKIY SE...KDAKL TLCLTKCGSQ ILGTVTVLAV NN.GSLNPIT NTVSTALVSL KFDASGVLLS S.STLDKEYW NFRK.GDVTP
ChAd9    EDDKLTLWTT PDPSPNCQIL AE...NDAKL TLCLTKCGSQ ILATVSVLVV GS.GDLNPIT GTVSSAQVFL RFDANGVLLT E.HSTLKKYW GYRQ.GDSID
ChAd10   EDDKLTLWTT PDPSPNCQIL AE...NDAKL TLCLTKCGSQ ILATVSVLVV GS.GNLNPIT GTVSSAQVFL RFDANGVLLT E.HSTLKKYW GYRQ.GDSID
ChAd4    EDDKLTLWTT PDPSPNCQIL AE...NDAKL TLCLTKCGSQ ILATVSVLVV GS.GNLNPIT GTVSSAQVFL RFDANGVLLT E.HSTLKKYW GYRQ.GDSID
CV68     EDDKLTLWTT PDPSPNCQIL AE...NDAKL TLCLTKCGSQ ILATVSVLVV GS.GNLNPIT GTVSSAQVFL RFDANGVLLT E.HSTLKKYW GYRQ.GDSID
ChAd16   EDDSLTLWTT PDPSPNCKIA SD...KDAKL TLCLTKCGSQ ILGTVSLLAV S..GSLAPIT GAVSTALVSL KFDANGALLE K.STLNREYW NYRQ.GDLIP

         501                                                                                                              600
C1       GTIT.SAKGF MPSTTAYPFI TYATQSLN.E DYIYGECYYK STNGTLFPLK VTVTLNRRMS AS....GMAY AMNFSWSLNA EEAPETTEVT LITSPFFFSY
ChAd11   GTAYTNAVGF MPNLTAYP.. ..KTQSQTAK SNIVSQVYLN GD..KSKPMI LTITLNGTNE TGD.ATVSTY SMSFSWNWNG S...NYINET FQTNSFTFSY
ChAd20   GTAYTNAVGF MPNLTAYP.. ..KTQSQTAK SNIVSQVYLN GD..KSKPMT LTITLNGTNE TGD.ATVSTY SMSFSWNWNG S...NYINET FQTNSFTFSY
ChAd17   AAPYTNAVGF MPNLAAYP.. ..KTQSQTAK NNIVSQVYLN GD..KSKPMT LTITLNGTNE SSETSQVSHY SMSFTWAWES G...QYATET FATNSFTFSY
ChAd3    AAPYTNAVGF MPNLAAYP.. ..KTQSQTAK NNIVSQVYLN GD..KSKPMT LTITLNGTNE SSETSQVSHY SMSFTWAWES G...QYATET FATNSFTFSY
ChAd19   ATPYTNAVGF MPNLAAYP.. ..KTQSQTAK NNIVSQVYLN GD..KSKPMT LTITLNGTNE SSETSQVSHY SMSFTWAWES G...QYATET FATNSFTFSY
PAN6     SVAYTNAVGF MPNIGAYP.. ..KTQSKTPK NSIVSQVYLT GE..TTMPMT LTITFNGTDE KDTT.PVSTY SMTFTWQWTG D..YKDKNIT FATNSFSFSY
ChAd5    GTPYTHAVGF MPNKKAYP.. ..KNTTAASK SHIVGDVYLD GD..ADKPLS LIITFNETDD ET.....CDY CINFQWKWGA D...QYKDKT LATSSFTFSY
ChAd6    ADPYTNAIGF MPNLNAYP.. ..KNTNAAAK SHIVGKVYLH GD..ESKPLD LIITFNETSD ES.....CTY CINFQWQWGT D...QYKDET LAVSSFTFSY
ChAd7    AEPYTNAIGF MPNLKAYP.. ..KNTSGAAK SHIVGKVYLH GD..TDKPLD LIITFNETSD ES.....CTY CINFQWKWDS T...KYTGET LATSSFTFSY
PAN5     AEAYTNAIGF MPNLKAYP.. ..KNTSGAAK SHIVGKVYLH GD..TGKPLD LIITFNETSD ES.....CTY CINFQWQWGA D...QYKNET LAVSSFTFSY
PAN7     AEPYTNAIGF MPNIKAYP.. ..KNTSAASK SHIVSQVYLN GD..EAKPLM LIITFNETED AT.....CTY SITFQWKWDS T...KYTGET LATSSFTFSY
ChAd9    GTPYANAVGF MPNLKAYP.. ..KSQSSTTK NNIVGQVYMN GD..VSKPML LTITLNGTDD SN.....STY SMSFSYTWTN G...SYVGAT FGANSYTFSY
ChAd10   GTPYTNAVGF MPNLKAYP.. ..KSQSSTTK NNIVGQVYMN GD..VSKPML LTITLNGTDD SN.....STY SMSFSYTWTN G...SYVGAT FGANSYTFSY
ChAd4    GTPYTNAVGF MPNLKAYP.. ..KSQSSTTK NNIVGQVYMN GD..VSKPML LTITLNGTDD SN.....STY SMSFSYTWTN G...SYVGAT FGANSYTFSY
CV68     GTPYTNAVGF MPNLKAYP.. ..KSQSSTTK NNIVGQVYMN GD..VSKPML LTITLNGTDD SN.....STY SMSFSYTWTN G...SYVGAT FGANSYTFSY
ChAd16   GTPYTHAVGF MPNKKAYP.. ..KNTTAASK SHIVGEVYLD GD..ADKPLS LIITFNETDD ES.....CDY CMNFQWKWGA D...QYKDKT LATSSFTFSY
```

Fig. 20C

```
601
      IREDD
C1
ChAd11 IAQE.
ChAd20 IAQE.
ChAd17 IAEQ.
ChAd3  IAEQ.
ChAd19 IAEQ.
PAN6   IAQE.
ChAd5  IAQE.
ChAd6  IAKE.
ChAd7  IAQE.
PAN5   IAKE.
PAN7   IAQE.
ChAd9  IAQE.
ChAd10 IAQE.
ChAd4  IAQE.
CV68   IAQE.
ChAd16 IAQE.
```

Fig. 20D

SEQ ID NO: 16


```
       1  ATGGCGACCC CATCGATGAT GCCGCAGTGG TCGTACATGC ACATCTCGGG
CCAGGACGCC

      61  TCGGAGTACC TGAGCCCCGG GCTGGTGCAG TTCGCCCGCG CCACCGAGAG
CTACTTCAGC

     121  CTGAGTAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGG

     181  TCTCAGCGCC TGACGCTGCG GTTCATTCCC GTGGACCGCG AGGACACCGC
GTACTCGTAC

     241  AAGGCGCGGT TCACCCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CTCCACCTAC

     301  TTTGACATCC GCGGGGTGCT GGACCGGGGT CCCACTTTCA AGCCCTACTC
TGGCACCGCC

     361  TACAACTCCC TGGCCCCCAA GGGCGCTCCC AACCCATGCG AGTGGGATGA
GGCTGCTACT

     421  GCCCTTGACA TTGATTTGAA CGCAGAAGAC GATGAAGAAA GCGACGAAGC
TCAAGGGGAA

     481  GCAGATCAGC AGAAAACTCA TGTATTTGGC CAGGCGCCCT ACTCCGGACA
GAACATTACA

     541  AAAGAAGGCA TACAGATAGG CATAGATGCT GCCAGTCAAG CCCAGACACC
TGTATATGCC

     601  GATAAAACAT TCCAACCAGA ACCTCAAGTT GGAGAATCAC AGTGGAATGA
GACAGAGATT

     661  AGTTATGGAG CGGGACGGGT GCTTAAAAAA ACCACTCTCA TGAAACCTTG
CTATGGGTCG

     721  TATGCAAGGC CTACTAATGA GAACGGAGGT CAGGGCATCC TCTTGGAACA
AGATGGAAAG

     781  AAAGAAAGTC AAGTGGAAAT GCAATTTTTC TCTACTACTC AGGCAGCCGC
GGGTAATTCA

     841  GATAATCCTA CCCCAAAGGT TGTTTTGTAC AGCGAGGATG TTAACCTGGA
AACACCAGAT

     901  ACACACATTT CATACATGCC CACCAACAAC GAGACAAATT CAAGAGAGCT
TTTGGGACAA

     961  CAGGCCATGC CCAACAGGCC TAATTACATT GGCTTCAGAG ACAACTTTAT
CGGTCTCATG

    1021  TATTACAACA GCACTGGCAA CATGGGAGTG CTTGCAGGTC AGGCCTCTCA
GTTGAACGCA

    1081  GTGGTGGACT TGCAAGACAG AAACACAGAA CTGTCATACC AGCTCTTGCT
TGATTCCATG
```

Fig. 21A

1141 GGTGACAGAA CCAGATACTT TTCCATGTGG AATCAGGCAG TGGACAGTTA
TGACCCAGAT

1201 GTCAGAATTA TTGAAAATCA TGGAACTGAA GACGAGCTCC CCAACTATTG
TTTCCCTCTG

1261 GGCGGCGTAA TCAATACGGA AACTTTCACA AAAGTAAAAC CTAAAGCTGC
ACAGGACGCT

1321 CAGTGGGAAA AAGATTCAGA ATTTTCAGAT AAAAATGAAA TAAGGGTGGG
AAACAACTTC

1381 GCCATGGAAA TTAACCTCAA TGCCAATCTG TGGAGGAACT TTTTGTACTC
CAACGTAGCC

1441 CTCTACTTGC CTGACAAGCT TAAGTATACT CCATCCAATG TGCAAATTTC
CAACAATCCC

1501 AACTCCTACG ATTACATGAA CAAGCGAGTG GTGGCCCCGG GGCTGGTGGA
CTGCTACATC

1561 AACCTGGGCG CGCGCTGGTC GCTGGACTAC ATGGACAACG TCAACCCCTT
CAACCACCAC

1621 CGCAATGCGG GCCTGCGCTA CCGCTCCATG CTCCTGGGCA ACGGGCGCTA
CGTGCCCTTC

1681 CACATCCAGG TGCCCCAGAA GTTCTTTGCC ATCAAGAACC TCCTCCTCCT
GCCGGGCTCC

1741 TACACCTACG AGTGGAACTT CAGGAAGGAT GTCAACATGG TCCTCCAGAG
CTCTCTGGGT

1801 AACGATCTCA GGGTGGACGG GGCCAGCATC AAGTTCGAGA GCATCTGCCT
CTACGCCACC

1861 TTCTTCCCCA TGGCCCACAA CACGGCCTCC ACGCTCGAGG CCATGCTCAG
GAACGACACC

1921 AACGACCAGT CCTTCAATGA CTACCTTTCC GCCGCCAACA TGCTCTACCC
CATACCCGCC

1981 AACGCCACCA ACGTCCCCAT CTCCATCCCC TCGCGCAACT GGGCGGCCTT
CCGCGGCTGG

2041 GCCTTCACCC GCCTCAAGAC CAAGGAGACC CCCTCCCTGG GCTCGGGATT
CGACCCCTAC

2101 TACACCTACT CGGGCTCCAT TCCCTACCTG GACGGCACCT TCTACCTCAA
CCACACTTTC

2161 AAGAAGGTCT CGGTCACCTT CGACTCCTCG GTCAGCTGGC CGGGCAACGA
CCGTCTGCTC

Fig. 21B

SEQ ID NO: 16

2221 ACCCCCAACG AGTTCGAGAT CAAGCGCTCG GTCGACGGGG AGGGCTACAA
CGTGGCCCAG

2281 TGCAACATGA CCAAGGACTG GTTCCTGGTC CAGATGCTGG CCAACTACAA
CATCGGCTAC

2341 CAGGGCTTCT ACATCCCAGA GAGCTACAAG GACAGGATGT ACTCCTTCTT
CAGGAACTTC

2401 CAGCCCATGA GCCGGCAGGT GGTGGACCAG ACCAAGTACA AGGACTACCA
GGAGGTGGGC

2461 ATCATCCACC AGCACAACAA CTCGGGCTTC GTGGGCTACC TCGCCCCCAC
CATGCGCGAG

2521 GGACAGGCCT ACCCCGCCAA CTTCCCCTAC CCGCTCATAG GCAAGACCGC
GGTCGACAGC

2581 ATCACCCAGA AAAAGTTCCT CTGCGACCGC ACCCTCTGGC GCATCCCCTT
CTCCAGCAAC

2641 TTCATGTCCA TGGGTGCGCT CTCGGACCTG GGCCAGAACT TGCTCTACGC
CAACTCCGCC

2701 CACGCCCTCG ACATGACCTT CGAGGTCGAC CCCATGGACG AGCCCACCCT
TCTCTATGTT

2761 CTGTTCGAAG TCTTTGACGT GGTCCGGGTC CACCAGCCGC ACCGCGGCGT
CATCGAGACC

2821 GTGTACCTGC GTACGCCCTT CTCGGCCGGC AACGCCACCA CCTAA

Fig. 21C

```
       1  ATGGCCACCC CATCGATGCT GCCCCAGTGG GCGTACATGC ACATCGCCGG
ACAGGACGCT

      61  TCGGAGTACC TGAGTCCGGG TCTGGTGCAG TTCGCCCGCG CCACAGACAC
CTACTTCAGT

     121  CTGGGGAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGC

     181  AGCCAGCGGC TGACGCTGCG CTTCGTGCCC GTGGACCGCG AGGACAACAC
CTACTCGTAC

     241  AAAGTGCGCT ACACGCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CAGCACCTAC

     301  TTTGACATCC GCGGCGTGCT GGATCGGGGC CCTAGCTTCA AACCCTACTC
CGGCACCGCC

     361  TACAACAGCC TGGCTCCCAA GGGAGCGCCC AATTCCAGCC AGTGGGAGCA
AAAAAAGACT

     421  GGCAATAATG CCAATGGAGA TACGGAGAAT GTCACTTATG GTGTAGCTGC
CATGGGAGGA

     481  ATTGACATCG ATAAAAATGG CCTTCAAATT GGAACCGATG ACACCAAAGA
TGACGATAAT

     541  GAAATTTATG CAGACAAAAC ATATCAGCCT GAGCCGCAAA TAGGAGAGGA
AAACTGGCAA

     601  GAAACATATT CCTACTATGG AGGTAGAGCT CTTAAAAAAG ATACCAAAAT
GAAGCCATGC

     661  TATGGCTCAT TTGCCAGACC TACCAATGTG AAAGGAGGAC AGGCAAAAAT
AAAAACAGAT

     721  GGAGATGTTA AGTCATTTGA CATAGACCTA GCCTTCTTTG ATATTCCCAA
TTCTGGCGCG

     781  GGAAATGGCA CAAATGTTAA CGATGATCCA GATATGGTTA TGTATACAGA
AAATGTAAAT

     841  CTGGAAACCC CAGATACTCA TATTGTGTAC AAACCAGGAA CTTCAGATGA
CAGCTCAAAG

     901  GTCAACTTGT GTCAGCAATC CATGCCTAAC AGACCCAATT ATATTGGCTT
CAGAGACAAT

     961  TTTATTGGGC TTATGTACTA CAACAGCACT GGCAATATGG GTGTGCTGGC
TGGTCAGGCC

    1021  TCTCAACTGA ATGCCGTGGT GGACTTGCAA GACAGAAACA CAGAGCTGTC
CTACCAGCTC

    1081  TTGCTTGACT CTCTGGGTGA CAGAACCAGG TATTTCAGTA TGTGGAATCA
GGCGGTGGAC
```

Fig. 22A

1141 AGTTATGATC CTGATGTGCG CATTATTGAA AACCATGGTG TGGAGGATGA
ATTGCCAAAC

1201 TATTGCTTCC CCTTGGATGG AGCAGGCACC AATTCGGTTT ACCAAGGTGT
TAAACCAAAA

1261 ACTGACAATG GCAACGATCA GTGGGAAACA GATTCCACAG TTTCAAGTCA
CAATCAGATA

1321 TGCAAAGGCA ATATCTATGC CATGGAGATC AACCTCCAGG CCAACCTGTG
GAGAAGTTTT

1381 CTCTACTCGA ACGTGGCCCT GTACCTGCCC GATTCTTACA AGTACACGCC
GGCCAACATC

1441 ACCCTGCCCA CCAACACCAA CACCTACGAT TACATGAACG GGAGAGTGGT
GCCTCCCTCG

1501 CTGGTGGACG CCTACATCAA CATCGGGGCG CGCTGGTCGC TGGACCCCAT
GGACAACGTG

1561 AATCCCTTCA ACCACCACCG CAACGCGGGC CTGCGCTACC GCTCCATGCT
CCTGGGCAAC

1621 GGGCGCTACG TGCCCTTCCA CATCCAGGTG CCCCAGAAAT TTTTCGCCAT
CAAGAGCCTC

1681 CTGCTCCTGC CCGGGTCCTA CACCTACGAG TGGAACTTCC GCAAGGACGT
CAACATGATC

1741 CTGCAGAGCT CCCTCGGCAA CGACCTGCGC ACGGACGGGG CCTCCATCTC
CTTCACCAGC

1801 ATCAACCTCT ACGCCACCTT CTTCCCCATG GCGCACAACA CGGCCTCCAC
GCTCGAGGCC

1861 ATGCTGCGCA ACGACACCAA CGACCAGTCC TTCAACGACT ACCTCTCGGC
GGCCAACATG

1921 CTCTACCCCA TCCCGGCCAA CGCCACCAAC GTGCCCATCT CCATCCCCTC
GCGCAACTGG

1981 GCCGCCTTCC GCGGCTGGTC CTTCACGCGC CTCAAGACCC GCGAGACGCC
CTCGCTGGGC

2041 TCCGGGTTCG ACCCCTACTT CGTCTACTCG GGCTCCATCC CCTACCTCGA
CGGCACCTTC

2101 TACCTCAACC ACACCTTCAA GAAGGTCTCC ATCACCTTCG ACTCCTCCGT
CAGCTGGCCC

2161 GGCAACGACC GCCTCCTGAC GCCCAACGAG TTCGAAATCA AGCGCACCGT
CGACGGAGAG

2221 GGATACAACG TGGCCCAGTG CAACATGACC AAGGACTGGT TCCTGGTCCA
GATGCTGGCC

Fig. 22B

2281 CACTACAACA TCGGCTACCA GGGCTTCTAC GTGCCCGAGG GCTACAAGGA
CCGCATGTAC

2341 TCCTTCTTCC GCAACTTCCA GCCCATGAGC CGCCAGGTGG TGGACGAGGT
CAACTACAAG

2401 GACTACCAGG CCGTCACCCT GGCCTACCAG CACAACAACT CGGGCTTCGT
CGGCTACCTC

2461 GCGCCCACCA TGCGCCAGGG CCAGCCCTAC CCCGCCAACT ACCCGTACCC
GCTCATCGGA

2521 AAGAGCGCCG TCACCAGCGT CACCCAGAAA AAGTTCCTCT GCGACAGGGT
CATGTGGCGC

2581 ATCCCCTTCT CCAGCAACTT CATGTCCATG GGCGCGCTCA CCGACCTCGG
CCAGAACATG

2641 CTCTATGCCA ACTCCGCCCA CGCGCTAGAC ATGAATTTCG AAGTCGACCC
CATGGATGAG

2701 TCCACCCTTC TCTATGTTGT CTTCGAAGTC TTCGACGTCG TCCGAGTGCA
CCAGCCCCAC

2761 CGCGGCGTCA TCGAGGCCGT CTACCTGCGC ACCCCCTTCT CGGCCGGTAA
CGCCACCACC

2821 TAA

Fig. 22C

```
    1  ATGGCCACCC CATCGATGCT GCCCCAGTGG GCGTACATGC ACATCGCCGG
ACAGGACGCT

   61  TCGGAGTACC TGAGTCCGGG TCTGGTGCAG TTCGCCCGCG CCACAGACAC
CTACTTCAGT

  121  CTGGGGAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGC

  181  AGCCAGCGGC TGACGCTGCG CTTCGTGCCC GTGGACCGCG AGGACAACAC
CTACTCGTAC

  241  AAAGTGCGCT ACACGCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CAGCACCTAC

  301  TTTGACATCC GCGGCGTGCT GGATCGGGGC CCTAGCTTCA AACCCTACTC
CGGCACCGCC

  361  TACAACAGCC TGGCTCCCAA GGGAGCGCCC AATTCCAGCC AGTGGGAGCA
AAAAAAGACT

  421  GGCAATAATG CCAATGGAGA TACGGAGAAT GTCACTTATG GTGTAGCTGC
CATGGGAGGA

  481  ATTGACATCG ATAAAAATGG CCTTCAAATT GGAACCGATG ACACCAAAGA
TGACGATAAT

  541  GAAATTTATG CAGACAAAAC ATATCAGCCT GAGCCGCAAA TAGGAGAGGA
AAACTGGCAA

  601  GAAACATATT CCTACTATGG AGGTAGAGCT CTTAAAAAAG ATACCAAAAT
GAAGCCATGC

  661  TATGGCTCAT TTGCCAGACC TACCAATGTG AAAGGAGGAC AGGCAAAAAT
AAAAACAGAT

  721  GGAGATGTTA AGTCATTTGA CATAGACCTA GCCTTCTTTG ATATTCCCAA
TTCTGGCGCG

  781  GGAAATGGCA CAAATGTTAA CGATGATCCA GATATGGTTA TGTATACAGA
AAATGTAAAT

  841  CTGGAAACCC CAGATACTCA TATTGTGTAC AAACCAGGAA CTTCAGATGA
CAGCTCAAAG

  901  GTCAACTTGT GTCAGCAATC CATGCCTAAC AGACCCAATT ATATTGGCTT
CAGAGACAAT

  961  TTTATTGGGC TTATGTACTA CAACAGCACT GGCAATATGG GTGTGCTGGC
TGGTCAGGCC

 1021  TCTCAACTGA ATGCCGTGGT GGACTTGCAA GACAGAAACA CAGAGCTGTC
CTACCAGCTC

 1081  TTGCTTGACT CTCTGGGTGA CAGAACCAGG TATTTCAGTA TGTGGAATCA
GGCGGTGGAC
```

Fig. 23A

1141 AGTTATGATC CTGATGTGCG CATTATTGAA AACCATGGTG TGGAGGATGA
ATTGCCAAAC

1201 TATTGCTTCC CCTTGGATGG AGCAGGCACC AATTCGGTTT ACCAAGGTGT
TAAACCAAAA

1261 ACTGACAATG GCAACGATCA GTGGGAAACA GATTCCACAG TTTCAAGTCA
CAATCAGATA

1321 TGCAAAGGCA ATATCTATGC CATGGAGATC AACCTCCAGG CCAACCTGTG
GAGAAGTTTT

1381 CTCTACTCGA ACGTGGCCCT GTACCTGCCC GATTCTTACA AGTACACGCC
GGCCAACATC

1441 ACCCTGCCCA CCAACACCAA CACCTACGAT TACATGAACG GGAGAGTGGT
GCCTCCCTCG

1501 CTGGTGGACG CCTACATCAA CATCGGGGCG CGCTGGTCGC TGGACCCCAT
GGACAACGTG

1561 AATCCCTTCA ACCACCACCG CAACGCGGGC CTGCGCTACC GCTCCATGCT
CCTGGGCAAC

1621 GGGCGCTACG TGCCCTTCCA CATCCAGGTG CCCCAGAAAT TTTTTGCCAT
CAAGAGCCTC

1681 CTGCTCCTGC CCGGGTCCTA CACCTACGAG TGGAACTTCC GCAAGGACGT
CAACATGATC

1741 CTGCAGAGCT CCCTCGGCAA CGACCTGCGC ACGGACGGGG CCTCCATCTC
CTTCACCAGC

1801 ATCAACCTCT ACGCCACCTT CTTCCCCATG GCGCACAACA CGGCCTCCAC
GCTCGAGGCC

1861 ATGCTGCGCA ACGACACCAA CGACCAGTCC TTCAACGACT ACCTCTCGGC
GGCCAACATG

1921 CTCTACCCCA TCCCGGCCAA CGCCACCAAC GTGCCCATCT CCATCCCCTC
GCGCAACTGG

1981 GCCGCCTTCC GCGGCTGGTC CTTCACGCGC CTCAAGACCC GCGAGACGCC
CTCGCTGGGC

2041 TCCGGGTTCG ACCCCTACTT CGTCTACTCG GGCTCCATCC CCTACCTCGA
CGGCACCTTC

2101 TACCTCAACC ACACCTTCAA GAAGGTCTCC ATCACCTTCG ACTCCTCCGT
CAGCTGGCCC

2161 GGCAACGACC GCCTCCTGAC GCCCAACGAG TTCGAAATCA AGCGCACCGT
CGACGGAGAG

2221 GGATACAACG TGGCCCAGTG CAACATGACC AAGGACTGGT TCCTGGTCCA
GATGCTGGCC

Fig. 23B

2281 CACTACAACA TCGGCTACCA GGGCTTCTAC GTGCCCGAGG GCTACAAGGA
CCGCATGTAC

2341 TCCTTCTTCC GCAACTTCCA GCCCATGAGC CGCCAGGTCG TGGACGAGGT
CAACTACAAG

2401 GACTACCAGG CCGTCACCCT GGCCTACCAG CACAACAACT CGGGCTTCGT
CGGCTACCTC

2461 GCGCCCACCA TGCGCCAGGG CCAGCCCTAC CCCGCCAACT ACCCCTACCC
GCTCATCGGC

2521 AAGAGCGCCG TCGCCAGCGT CACCCAGAAA AAGTTCCTCT GCGACCGGGT
CATGTGGCGC

2581 ATCCCCTTCT CCAGCAACTT CATGTCCATG GGCGCGCTCA CCGACCTCGG
CCAGAACATG

2641 CTCTACGCCA ACTCCGCCCA CGCGCTAGAC ATGAATTTCG AAGTCGACCC
CATGGATGAG

2701 TCCACCCTTC TCTATGTTGT CTTCGAAGTC TTCGACGTCG TCCGAGTGCA
CCAGCCCCAC

2761 CGCGGCGTCA TCGAGGCCGT CTACCTGCGC ACCCCCTTCT CGGCCGGTAA
AGCCACCACC

2821 TAA

Fig. 23C

```
        1  ATGGCCACCC CATCGATGCT GCCCCAGTGG GCGTACATGC ACATCGCCGG
ACAGGACGCT

       61  TCGGAGTACC TGAGTCCGGG TCTGGTGCAG TTCGCCCGCG CCACAGACAC
CTACTTCAGT

      121  CTGGGGAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGC

      181  AGCCAGCGGC TGACGCTGCG CTTCGTGCCC GTGGACCGCG AGGACAACAC
CTACTCGTAC

      241  AAAGTGCGCT ACACGCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CAGCACCTAC

      301  TTTGACATCC GCGGCGTGCT GGACCGGGGC CCTAGCTTCA AACCTTACTC
CGGCACCGCT

      361  TACAACAGCC TGGCCCCCAA GGGAGCACCC AATTCCAGCC AGTGGGAGCA
AAAAAAGACT

      421  GGCAAAAATG CCAATGGAGA TACGGAGAAT GTCACTTATG GTGTAGCTGC
CATGGGAGGA

      481  ATTGACATCG ATAAAAATGG CCTTCAAATT GGAACCGATG ACACCAAAGA
TGGCGATAAT

      541  GAAATTTATG CAGACAAAAC ATATCAGCCT GAGCCGCAAA TAGGAGAGGA
AAACTGGCAA

      601  GAAACATATT CCTACTATGG AGGTAGAGCT CTTAAAAAAG ATACCAAAAT
GAAGCCATGC

      661  TATGGCTCAT TTGCTAGACC TACCAATGTG AAAGGAGGAC AGGCAAAAAT
AAAAACAGAT

      721  GGAGATGTTA AGTCATTTGA CATAGACCTA GCCTTCTTTG ATATTCCAAA
TTCTGGCGCG

      781  GGAAATGGCA CAAATGTTAA CGATGATCCA GATATGGTTA TGTATACAGA
AAATGTAAAT

      841  CTGGAAACCC CAGATACTCA TATTGTGTAC AAACCAGGAA CTTCAGATGA
CAGCTCCGAG

      901  GTCAACTTGT GTCAGCAATC CATGCCTAAC AGACCCAATT ATATTGGCTT
CAGAGACAAT

      961  TTTATTGGGC TTATGTACTA CAACAGCACT GGCAATATGG GTGTGCTGGC
TGGTCAGGCC

     1021  TCTCAACTGA ATGCCGTGGT GGACTTGCAA GACAGAAACA CAGAGCTGTC
CTACCAGCTC

     1081  TTGCTTGACT CTCTGGGTGA CAGAACCAGG TATTTCAGTA TGTGGAATCA
GGCGGTGGAC
```

Fig. 24A

1141 AGTTATGATC CTGATGTGCG CATTATTGAA AACCATGGTG TGGAGGATGA
ATTGCCAAAC

1201 TATTGCTTCC CCTTGGATGG AGCAGGCACC AATTCGGTTT ACCAAGGTGT
TAAACCAAAA

1261 ACTGACAATG GCAACGATCA GTGGGAAACA GATTCCACAG TTTCAAGTCA
CAATCAGATA

1321 TGCAAAGGCA ATATCTATGC CATGGAGATC AATCTCCAGG CCAACCTGTG
GAGAAGTTTC

1381 CTCTACTCGA ACGTGGCCCT GTACCTGCCC GATTCTTACA AGTACACGCC
GGCCAACATC

1441 ACCCTGCCCA CCAACACCAA CACCTACGAT TACATGAACG GGAGAGTGGT
GCCTCCCTCG

1501 CTGGTGGATG CCTACATCAA CATCGGAGCG CGCTGGTCGC TGGACCCCAT
GGACAACGTC

1561 AATCCCTTCA ACCACCACCG CAATGCGGGG CTGCGCTACC GCTCCATGCT
CCTGGGCAAC

1621 GGGCGCTACG TGCCCTTCCA CATCCAGGTG CCCCAGAAAT TTTTCGCCAT
CAAGAGCCTT

1681 CTGCTCCTGC CCGGGTCCTA CACCTACGAG TGGAACTTCC GCAAGGACGT
CAACATGATC

1741 CTGCAGAGCT CCCTCGGCAA CGACCTGCGC ACGGACGGGG CCTCCATCTC
CTTCACCAGC

1801 ATCAACCTCT ACGCCACCTT CTTCCCCATG GCGCACAACA CGGCCTCCAC
GCTCGAGGCC

1861 ATGCTGCGCA ACGACACCAA CGACCAGTCC TTCAACGACT ACCTCTCGGC
GGCCAACATG

1921 CTCTACCCCA TCCCGGCCAA CGCCACCAAC GTGCCCATCT CCATCCCCTC
GCGCAACTGG

1981 GCCGCCTTCC GCGGCTGGTC CTTCACGCGC CTCAAGACCA AGGAGACGCC
CTCGCTGGGC

2041 TCCGGGTTCG ACCCATACTT CGTCTACTCG GGCTCCATCC CCTACCTCGA
CGGCACCTTC

2101 TACCTCAACC ACACCTTCAA GAAGGTCTCC ATCACCTTCG ATTCCTCCGT
CAGCTGGCCC

2161 GGCAACGACC GGCTCCTGAC GCCCAACGAG TTCGAAATCA AGCGCACCGT
CGACGGCGAG

2221 GGATACAACG TGGCCCAGTG CAACATGACC AAGGACTGGT TCCTGGTCCA
GATGCTGGCC

Fig. 24B

2281 CACTACAACA TCGGCTACCA GGGCTTCTAC GTGCCCGAGG GCTACAAGGA
CCGCATGTAC

2341 TCCTTCTTCC GCAACTTCCA GCCCATGAGC CGCCAGGTGG TGGACGAGGT
CAACTACAAG

2401 GACTACCAGG CCGTCACCCT GGCCTACCAG CACAACAACT CGGGCTTCGT
CGGCTACCTC

2461 GCGCCCACCA TGCGCCAGGG CCAGCCCTAC CCCGCCAACT ACCCGTACCC
GCTCATCGGC

2521 AAGAGCGCCG TCACCAGCGT CACCCAGAAA AAGTTCCTCT GCGACAGGGT
CATGTGGCGC

2581 ATCCCCTTCT CCAGCAACTT CATGTCCATG GGCGCGCTCA CCGACCTCGG
GCAGAACATG

2641 CTCTATGCCA ACTCCGCCCA CGCGCTAGAC ATGAATTTCG AAGTCGACCC
CATGGATGAG

2701 TCCACCCTTC TCTATGTTGT CTTCGAAGTC TTCGACGTCG TCCGAGTGCA
CCAGCCCCAC

2761 CGCGGCGTCA TCGAGGCCGT CTACCTGCGC ACCCCCTTCT CGGCCGGTAA
CGCCACCACC

2821 TAA

Fig. 24C

1 ATGGCCACCC CATCGATGCT GCCCCAGTGG GCGTACATGC ACATCGCCGG ACAGGACGCT

61 TCGGAGTACC TGAGTCCGGG TCTGGTGCAG TTCGCCCGCG CCACAGACAC CTACTTCAGT

121 CTGGGGAACA AGTTTAGGAA CCCCACGGTG GCACCCACGC ACGATGTGAC CACCGACCGC

181 AGCCAGCGGC TGACGCTGCG CTTCGTGCCC GTGGACCGCG AGGACAACAC CTACTCGTAC

241 AAAGTGCGCT ACACGCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC CAGCACCTAC

301 TTTGACATCC GCGGCGTGCT GGATCGGGGC CCTAGCTTCA AACCCTACTC CGGCACCGCT

361 TACAACAGCC TGGCTCCCAA GGGAGCGCCC AACACTTGCC AGTGGACATA TACTGATAAC

421 CAAACTGAGA AAACAGCCAC ATATGGAAAT GCACCCGTAG AGGGCATTAA CATTACAAAA

481 GATGGCATTC AACTTGGAAC TGACAGCGAT GGTCAGGCAA TCTATGCAGA CGAAACTTAT

541 CAGCCCGAAC CTCAGGTGGG AGATCCTGAA TGGCATGATA CCACAGGTAC AGAAGAAAAA

601 TATGGAGGCA GAGCGCTTAA ACCTGCCACC GACATGAAAC CTTGCTATGG CTCTTTTGCC

661 AAGCCAACTA ATGTTAAGGG AGGTCAGGCC AAAAGCAGAA CAAAAACTGA TGGAACAACT

721 GAGCCTGATA TTGACATGGC CTTTTTTGAT GGCAGAAATG CAACAACAGC TGGTTTGACT

781 CCAGAAATTG TTTTGTATAC TGAAAATGTG GATCTGGAAA CTCCAGATAC CCATATTGTA

841 TACAAGGCAG GCACAGATGA CAGCAGCTCT TCTATCAATT TGGGTCAGCA GTCCATGCCC

901 AACAGACCCA ACTACATTGG CTTCAGAGAC AACTTTATCG GGCTCATGTA CTACAACAGC

961 ACTGGCAATA TGGGTGTACT GGCTGGACAG GCCTCCCAGC TGAATGCTGT GGTGGACTTG

1021 CAGGACAGAA ACACTGAACT GTCCTACCAG CTCTTGCTTG ACTCTCTGGG TGACAGAACC

1081 AGGTATTTCA GTATGTGGAA TCAGGCGGTG GACAGTTATG ACCCCGATGT GCGCATTATT

Fig. 25A

1141 GAAAATCACG GTGTGGAGGA TGAACTCCCC AACTATTGCT TCCCCCTGAA
TGCTGTGGGT

1201 AGAACAAATA GTTATCAGGG AATTAAACCC AATGGAGGCG ATCCAGCTAC
ATGGGCCAAA

1261 GATGAAAGCG TCAATGATTC TAATGAATTG GGCAAGGGCA ATCCTTTCGC
CATGGAGATC

1321 AACATCCAGG CCAACCTGTG GCGGAACTTC CTCTACGCGA ACGTGGCGCT
GTACCTGCCC

1381 GACTCCTACA AGTACACGCC GGCCAACATC ACGCTGCCCG CCAACACCAA
CACCTACGAT

1441 TACATGAACG GCCGCGTGGT GGCGCCCTCG CTGGTGGACG CCTACATCAA
CATCGGGGCG

1501 CGCTGGTCGC TGGACCCCAT GGACAACGTC AACCCCTTCA ACCACCACCG
CAACGCGGGC

1561 CTGCGCTACC GCTCCATGCT CCTGGGCAAC GGGCGCTACG TGCCCTTCCA
CATCCAGGTG

1621 CCCCAAAAGT TTTTCGCCAT CAAGAGCCTC CTGCTCCTGC CCGGGTCCTA
CACCTACGAG

1681 TGGAACTTCC GCAAGGACGT CAACATGATC CTGCAGAGCT CCCTCGGCAA
CGACCTGCGC

1741 ACGGACGGGG CCTCCATCGC CTTCACCAGC ATCAACCTCT ACGCCACCTT
CTTCCCCATG

1801 GCGCACAACA CCGCCTCCAC GCTCGAGGCC ATGCTGCGCA ACGACACCAA
CGACCAGTCC

1861 TTCAACGACT ACCTCTCGGC GGCCAACATG CTCTACCCCA TCCCGGCCAA
CGCCACCAAC

1921 GTGCCCATCT CCATCCCCTC GCGCAACTGG GCCGCCTTCC GCGGATGGTC
CTTCACGCGC

1981 CTCAAGACCC GCGAGACGCC CTCGCTAGGC TCCGGGTTCG ACCCCTACTT
CGTCTACTCG

2041 GGCTCCATCC CCTACCTCGA CGGCACCTTC TACCTCAACC ACACCTTCAA
GAAGGTCTCC

2101 ATCACCTTCG ACTCCTCCGT CAGCTGGCCC GGCAACGACC GCCTCCTGAC
GCCCAACGAG

2161 TTCGAAATCA AGCGCACCGT CGACGGAGAG GGATACAACG TGGCCCAGTG
CAACATGACC

2221 AAGGACTGGT TCCTGGTCCA GATGCTGGCC CACTACAACA TCGGCTACCA
GGGCTTCTAC

Fig. 25B

2281 GTGCCCGAGG GCTACAAGGA CCGCATGTAC TCCTTCTTCC GCAACTTCCA
GCCCATGAGC

2341 CGCCAGGTCG TGGACGAGGT CAACTACAAG GACTACCAGG CCGTCACCCT
GGCCTACCAG

2401 CACAACAACT CGGGCTTCGT CGGCTACCTC GCGCCCACCA TGCGCCAGGG
CCAGCCCTAC

2461 CCCGCCAACT ACCCCTACCC GCTCATCGGC AAGAGCGCCG TCGCCAGCGT
CACCCAGAAA

2521 AAGTTCCTCT GCGACCGGGT CATGTGGCGC ATCCCCTTCT CCAGCAACTT
CATGTCCATG

2581 GGCGCGCTCA CCGACCTCGG CCAGAACATG CTCTACGCCA ACTCCGCCCA
CGCGCTAGAC

2641 ATGAATTTCG AAGTCGACCC CATGGATGAG TCCACCCTTC TCTATGTTGT
CTTCGAAGTC

2701 TTCGACGTCG TCCGAGTGCA CCAGCCCCAC CGCGGCGTCA TCGAGGCCGT
CTACCTGCGC

2761 ACGCCCTTCT CGGCCGGCAA CGCCACCACC TAA

Fig. 25C

SEQ ID NO: 21


```
      1  ATGGCCACCC CATCGATGCT GCCCCAGTGG GCGTACATGC ACATCGCCGG
ACAGGACGCT

     61  TCGGAGTACC TGAGTCCGGG TCTGGTGCAG TTCGCCCGCG CCACAGACAC
CTACTTCAGT

    121  CTGGGGAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGC

    181  AGCCAGCGGC TGACGCTGCG CTTCGTGCCC GTGGACCGCG AGGACAACAC
CTACTCGTAC

    241  AAAGTGCGCT ACACGCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CAGCACCTAC

    301  TTTGACATCC GCGGCGTGCT GGATCGGGGC CCTAGCTTCA AACCCTACTC
CGGCACCGCC

    361  TACAACAGCC TGGCTCCCAA GGGAGCGCCC AACACTTGCC AGTGGACATA
TACTGATAAC

    421  CAAACTGAGA AAACAGCCAC ATATGGAAAT GCGCCTGTGC AAGGCATTAG
TATTACAAAA

    481  GATGGTATTC AACTTGGAAC TGACACTGAT GATCAGCCCA TTTATGCAGA
TAAAACTTAT

    541  CAACCAGAGC CTCAAGTGGG TGATGCTGAA TGGCATGACA TCACTGGTAC
TGATGAAAAA

    601  TATGGAGGCA GAGCTCTCAA GCCTGACACC AAAATGAAGC CCTGCTATGG
TTCTTTTGCC

    661  AAGCCTACCA ATAAAGAAGG AGGTCAGGCA AATGTGAAAA CCGAAACAGG
CGGTACCAAA

    721  GAATATGACA TTGACATGGC ATTCTTCGAT AATCGAAGTG CAGCTGCGGC
TGGCCTGGCC

    781  CCAGAAATTG TTTTGTATAC TGAGAATGTG GATCTGGAAA CTCCAGATAC
TCATATTGTA

    841  TACAAGGCAG GCACAGATGA CAGCAGCTCT TCTATCAATT TGGGTCAGCA
GTCCATGCCC

    901  AACAGACCCA ACTACATTGG CTTCAGAGAC AACTTTATCG GTCTCATGTA
CTACAACAGC

    961  ACTGGCAATA TGGGTGTACT GGCTGGTCAG GCCTCCCAGC TGAATGCTGT
GGTGGACTTG

   1021  CAGGACAGAA ACACTGAACT GTCCTACCAG CTCTTGCTTG ACTCTCTGGG
TGACAGAACC

   1081  AGGTATTTTA GTATGTGGAA TCAGGCGGTG GACAGTTATG ACCCCGATGT
GCGCATTATT
```

Fig. 26A

1141 GAAAATCACG GTGTGGAGGA TGAACTCCCT AATTATTGCT TCCCCCTTAA
TGCTGTGGGT

1201 AGAACTGATA CTTACCAGGG AATTAAGGCC AATGGTGCTG ATCAAACCAC
ATGGACCAAA

1261 GATGATACTG TTAATGATGC TAATGAATTG GGCAAGGGCA ATCCTTTCGC
CATGGAGATC

1321 AACATCCAGG CCAACCTGTG GCGGAACTTC CTCTACGCGA ACGTGGCCCT
GTACCTGCCC

1381 GACTCCTACA AGTACACGCC GGCCAACATC ACGCTGCCCA CCAACACCAA
CACCTACGAT

1441 TACATGAACG GCCGCGTGGT GGCGCCCTCG CTGGTGGACG CCTACATCAA
CATCGGGGCG

1501 CGCTGGTCGC TGGACCCCAT GGACAACGTC AACCCCTTCA ACCACCACCG
CAACGCGGGC

1561 CTGCGCTACC GCTCCATGCT CCTGGGCAAC GGGCGCTACG TGCCCTTCCA
CATCCAGGTG

1621 CCCCAAAAGT TCTTCGCCAT CAAGAGCCTC CTGCTCCTGC CCGGGTCCTA
CACCTACGAG

1681 TGGAACTTCC GCAAGGACGT CAACATGATC CTGCAGAGCT CCCTCGGCAA
CGACCTGCGC

1741 ACGGACGGGG CCTCCATCGC CTTCACCAGC ATCAACCTCT ACGCCACCTT
CTTCCCCATG

1801 GCGCACAACA CCGCCTCCAC GCTCGAGGCC ATGCTGCGCA ACGACACCAA
CGACCAGTCC

1861 TTCAACGACT ACCTCTCGGC GGCCAACATG CTCTACCCCA TCCCGGCCAA
TGCCACCAAC

1921 GTGCCCATCT CCATCCCCTC GCGCAACTGG GCCGCCTTCC GCGGATGGTC
CTTCACGCGC

1981 CTCAAGACCC GCGAGACGCC CTCGCTAGGC TCCGGGTTCG ACCCCTACTT
CGTCTACTCG

2041 GGCTCCATCC CCTACCTCGA CGGCACCTTC TACCTCAACC ACACCTTCAA
GAAGGTCTCC

2101 ATCACCTTCG ACTCCTCCGT CAGCTGGCCC GGCAACGACC GCCTCCTGAC
GCCCAACGAG

2161 TTCGAAATCA AGCGCACCGT CGACGGAGAG GGGTACAACG TGGCCCAGTG
CAACATGACC

2221 AAGGACTGGT TCCTGGTCCA GATGCTGGCC CACTACAACA TCGGCTACCA
GGGCTTCTAC

Fig. 26B

2281 GTGCCCGAGG GCTACAAGGA CCGCATGTAC TCCTTCTTCC GCAACTTCCA
GCCCATGAGC

2341 CGCCAGGTCG TGGACGAGGT CAACTACAAG GACTACCAGG CCGTCACCCT
GGCCTACCAG

2401 CACAACAACT CGGGCTTCGT CGGCTACCTC GCGCCCACCA TGCGCCAGGG
CCAGCCCTAC

2461 CCCGCCAACT ACCCCTACCC GCTCATCGGC AAGAGCGCCG TCGCCAGCGT
CACCCAGAAA

2521 AAGTTCCTCT GCGACCGGGT CATGTGGCGC ATCCCCTTCT CCAGCAACTT
CATGTCCATG

2581 GGCGCGCTCA CCGACCTCGG CCAGAACATG CTCTACGCCA ACTCCGCCCA
CGCGCTAGAC

2641 ATGAATTTCG AAGTCGACCC CATGGATGAG TCCACCCTTC TCTATGTTGT
CTTCGAAGTC

2701 TTCGACGTCG TCCGAGTGCA CCAGCCCCAC CGCGGCGTCA TCGAGGCCGT
CTACCTGCGC

2761 ACGCCCTTCT CGGCCGGCAA CGCCACCACC TAA

Fig. 26C

```
   1  ATGGCGACCC CATCGATGAT GCCGCAGTGG TCGTACATGC ACATCTCGGG
CCAGGACGCC

  61  TCGGAGTACC TGAGTCCCGG GCTGGTGCAG TTCGCTCGCG CCACCGAGAG
CTACTTCAGT

 121  CTGAGTAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGG

 181  TCCCAGCGCC TGACGCTGCG GTTCATCCCC GTGGACCGCG AGGACACCGC
GTACTCGTAC

 241  AAGGCGCGGT TCACCCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CTCCACCTAC

 301  TTTGACATCC GCGGCGTGCT GGACCGCGGC CCCACCTTCA AGCCCTACTC
CGGCACCGCY

 361  TACAACTCCC TGGCCCCCAA GGGCGCTCCC AACTCCTGCG AGTGGGAGCA
AGAGGAAACT

 421  CAGGCAGTTG AAGAAGCAGC AGAAGAGGAG GAAGAAGATG CTGACGGTCA
AGCTGAGGAA

 481  GAGCAAGCAG CTACCAAAAA GACTCATGTA TATGCTCAGG CTCCCCTTTC
CGGCGAAAAA

 541  ATTAGCAAAG ACGGTCTGCA GATAGGAACG GACGCTACAG CAACCGAACA
AAAACCTATT

 601  TATGCAGACC CTACATTCCA GCCCGAACCC CAAATCGGGG AGTCCCAGTG
GAATGAGGCA

 661  GATGCTACAG TCGCTGGTGG TAGAGTGCTC AAGAAAACCA CTCCCATGAA
ACCATGCTAT

 721  GGTTCCTATG CAAGACCCAC GAATGCTAAT GGAGGTCAGG GTGTACTAGC
GGCAAATGCC

 781  CAAGGACAGC TAGAATCTCA GGTTGAAATG CAATTCTTTT CAACTTCTGA
AAACGCCCGT

 841  AACGAGGCTA ACAACATTCA GCCCAAATTG GTGCTGTATA GCGAGGATGT
GCACATGGAG

 901  ACCCCGGATA CACACCTCTC TTACAAGCCC ACAAAAAGCG ATGACAATTC
TAAAGTTATG

 961  CTGGGCCAAC AGGCCATGCC CAACAGGCCT AATTACATTG GCTTCAGAGA
CAACTTTATC

1021  GGTCTCATGT ACTACAACAG CACTGGCAAC ATGGGAGTGC TTGCAGGTCA
GGCCTCTCAG

1081  TTGAATGCAG TGGTGGACTT GCAAGACAGA AACACAGAAC TGTCCTACCA
GCTCTTGCTT
```

Fig. 27A

1141 GATTCCATGG GTGACAGAAC CAGATATTTC TCCATGTGGA ATCAGGCAGT
GGACAGTTAT

1201 GACCCAGATG TCAGAATTAT TGAAAATCAT GGAACTGAAG ACGAGCTCCC
CAACTATTGT

1261 TTCCCTCTGG GCGGCATAGG GGTAACTGAC ACTTACCAGG CTGTTAAGAC
CAACAATGGC

1321 AATAATGGGG GTCAGGTGAC TTGGACAAAA GATGAAACTT TTGCAGAGCG
CAATGAGATA

1381 GGGGTGGGAA ACAATTTCGC CATGGAGATC AACCTCAATG CCAACCTGTG
GAGGAACTTC

1441 CTGTACTCCA ACGTGGCCCT GTACCTGCCA GACAAGCTTA AGTACAACCC
CTCCAACGTG

1501 GACATCTCTG ACAACCCCAA CACCTACGAT TACATGAACA AGCGAGTGGT
GGCCCCGGGG

1561 CTGGTGGACT GCTACATCAA CCTGGGCGCG CGCTGGTCGC TGGACTACAT
GGACAACGTC

1621 AACCCTTTCA ACCACCACCG CAACGCGGGC CTGCGCTACC GCTCCATGCT
CCTGGGCAAC

1681 GGGCGCTACG TGCCCTTCCA CATCCAGGTG CCCCAGAAGT TCTTTGCCAT
CAAGAACCTC

1741 CTCCTCCTGC CGGGCTCCTA CACCTACGAG TGGAACTTCA GGAAGGATGT
CAACATGGTC

1801 CTCCAGAGCT CTCTGGGCAA CGATCTCAGG GTGGACGGGG CCAGCATCAA
GTTCGAGAGC

1861 ATCTGCCTCT ACGCCACCTT CTTCCCCATG GCCCACAACA CCGCCTCCAC
GCTCGAGGCC

1921 ATGCTCAGGA ACGACACCAA CGACCAGTCC TTCAATGACT ACCTCTCCGC
CGCCAACATG

1981 CTCTACCCCA TCCCCGCCAA CGCCACCAAC GTCCCCATCT CCATCCCCTC
GCGCAACTGG

2041 GCGGCCTTCC GCGGCTGGGC CTTCACCCGC CTCAAGACCA AGGAGACCCC
CTCCCTGGGC

2101 TCGGGATTCG ACCCCTACTA CACCTACTCG GGATCCATTC CCTACCTGGA
CGGCACCTTC

2161 TACCTCAACC ACACTTTCAA GAAGGTCTCG GTCACCTTCG ACTCCTCGGT
CAGCTGGCCG

2221 GGCAACGACC GCCTGCTCAC CCCCAACGAG TTCGAGATCA AGCGCTCGGT
CGACGGGGAG

Fig. 27B

2281 GGCTACAACG TGGCCCAGTG CAACATGACC AAGGACTGGT TCCTGGTCCA
GATGCTGGCC

2341 AACTACAACA TCGGCTACCA GGGCTTCTAC ATCCCAGAGA GCTACAAGGA
CAGGATGTAC

2401 TCCTTCTTCA GGAACTTCCA GCCCATGAGC CGGCAGGTGG TGGACCAGAC
CAAGTACAAG

2461 GACTACCAGG AGGTGGGCAT CATCCACCAG CACAACAACT CGGGCTTCGT
GGGCTACCTC

2521 GCCCCCACCA TGCGCGAGGG ACAGGCCTAC CCCGCCAACT TCCCCTACCC
GCTCATAGGC

2581 AAGACCGCGG TCGACAGCAT CACCCAGAAA AAGTTCCTCT GCGACCGCAC
CCTCTGGCGC

2641 ATCCCCTTCT CCAGCAACTT CATGTCCATG GGTGCGCTCA CGGACCTGGG
CCAGAACCTG

2701 CTCTATGCCA ACTCCGCCCA CGCGCTCGAC ATGACCTTCG AGGTCGACCC
CATGGACGAG

2761 CCCACCCTTC TCTATGTTCT GTTCGAAGTC TTTGACGTGG TCCGGGTCCA
CCAGCCGCAC

2821 CGCGGCGTCA TCGAGACCGT GTACCTGCGC ACGCCCTTCT CGGCCGGCAA
CGCCACCACC

2881 TAA

Fig. 27C

SEQ ID NO: 23

```
   1  ATGGCCACCC CATCGATGCT GCCCCAGTGG GCGTACATGC ACATCGCCGG
ACAGGACGCT

  61  TCGGAGTACC TGAGTCCGGG TCTGGTGCAG TTCGCCCGCG CCACAGACAC
CTACTTCAGT

 121  CTGGGGAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGC

 181  AGCCAGCGGC TGACGCTGCG CTTCGTGCCC GTGGACCGCG AGGACAACAC
CTACTCGTAC

 241  AAAGTGCGCT ACACGCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CAGCACCTAC

 301  TTTGACATCC GCGGCGTGCT GGACCGGGGC CCTAGCTTCA AACCCTACTC
CGGCACCGCC

 361  TACAACAGCC TGGCCCCCAA GGGAGCTCCC AATTCCAGTC AGTGGGAGCA
GACGGAGAAC

 421  GGGGGCGGAC AGGCTACGAC TAAAACACAC ACCTATGGAG TTGCCCCAAT
GGGTGGAACT

 481  AATATTACAG TCGACGGACT ACAAATTGGA ACTGACGCTA CAGCTGATAC
GGAAAAACCA

 541  ATTTATGCTG ATAAAACATT CCAACCTGAG CCTCAGATAG GAGAGGAAAA
CTGGCAAGAA

 601  ACTGAAAGCT TTTATGGCGG TAGGGCTCTT AAGAAAGACA CAAACATGAA
GCCTTGTTAT

 661  GGCTCATTTG CCAGACCTAC CAATGAAAAG GGAGGTCAAG CTAAACTTAA
AGTTGGAGCT

 721  GATGGGCTGC CGACCAAAGA ATTTGACATA GACCTAGCAT TCTTTGATAC
TCCTGGTGGC

 781  ACTGTGACCG GAGGTACAGA GGAGTATAAA GCAGATATTG TTATGTATAC
CGAAAACACG

 841  TATCTGGAAA CTCCAGACAC ACATGTGGTG TATAAACCAG GCAAGGATAA
CACAAGTTCT

 901  AAAATTAACC TGGTCCAGCA GTCTATGCCC AACAGGCCCA ACTACATTGG
GTTTAGGGAC

 961  AACTTTATTG GGCTCATGTA TTACAACAGC ACTGGCAATA TGGGTGTGCT
GGCCGGTCAG

1021  GCTTCTCAGT TGAATGCTGT GGTTGACTTG CAAGACAGAA ACACTGAACT
GTCTTACCAG

1081  CTCTTGCTTG ACTCTTTGGG TGACAGAACC AGGTATTTCA GTATGTGGAA
TCAGGCGGTG
```

Fig. 28A

SEQ ID NO: 23

1141 GACAGTTATG ATCCTGATGT GCGCATTATT GAAAACCATG GTGTGGAAGA TGAACTTCCC

1201 AACTATTGCT TCCCCCTGGA TGGGTCTGGC ACTAACGCCG CTTACCAAGG TGTGAAAGTA

1261 AAAAATGGTC AAGATGGTGA TGTTGAGAGC GAATGGGAAA AAGATGATAC TGTCGCAGCT

1321 CGAAATCAAT TATGCAAGGG CAACATTTTT GCCATGGAGA TCAATCTCCA GGCCAACCTG

1381 TGGAGAAGTT TTCTCTACTC GAACGTGGCC CTGTACCTGC CCGATTCTTA CAAGTACACG

1441 CCGGCCAACA TCACCCTGCC CACCAACACC AACACCTACG ATTACATGAA CGGGAGAGTG

1501 GTGCCTCCCT CGCTGGTGGA CGCCTACATC AACATCGGGG CGCGCTGGTC GCTGGACCCC

1561 ATGGACAACG TCAATCCCTT CAACCACCAT CGCAACGCGG GGCTGCGCTA CCGCTCCATG

1621 CTCCTGGGCA ACGGGCGCTA CGTGCCCTTC CACATCCAGG TGCCCCAGAA ATTTTTCGCC

1681 ATTAAGAGCC TCCTGCTCCT GCCCGGGTCC TACACCTACG AGTGGAACTT CCGCAAGGAC

1741 GTCAACATGA TCCTGCAGAG CTCCCTCGGC AACGACCTGC GCACGGACGG GGCCTCCATC

1801 TCCTTCACCA GCATCAACCT CTACGCCACC TTCTTCCCCA TGGCGCACAA CACCGCCTCC

1861 ACGCTCGAGG CCATGCTGCG CAACGACACC AACGACCAGT CCTTCAACGA CTACCTCTCG

1921 GCGGCCAACA TGCTCTACCC CATCCCGGCC AACGCCACCA ACGTGCCCAT CTCCATCCCC

1981 TCGCGCAACT GGGCCGCCTT CCGCGGCTGG TCCTTCACGC GCCTCAAGAC CAAGGAGACG

2041 CCCTCGCTGG GCTCCGGGTT CGACCCCTAC TTCGTCTACT CGGGCTCCAT CCCCTACCTC

2101 GACGGCACCT TCTACCTCAA CCACACCTTC AAGAAGGTCT CCATCACCTT CGACTCCTCC

2161 GTCAGCTGGC CCGGCAACGA CCGGCTCCTG ACGCCCAACG AGTTCGAAAT CAAGCGCACC

2221 GTCGACGGCG AGGGCTACAA CGTGGCCCAG TGCAACATGA CCAAGGACTG GTTCCTGGTC

2281 CAGATGCTGG CCCACTACAA CATCGGCTAC CAGGGCTTCT ACGTGCCCGA GGGCTACAAG

Fig. 28B

SEQ ID NO: 23

2341 GACCGCATGT ACTCCTTCTT CCGCAACTTC CAGCCCATGA GCCGCCAGGT CGTGGACGAG

2401 GTCAACTACA AGGACTACCA GGCCGTCACC CTGGCCTACC AGCACAACAA CTCGGGCTTC

2461 GTCGGCTACC TCGCGCCCAC CATGCGCCAG GGCCAGCCCT ACCCCGCCAA CTACCCCTAC

2521 CCGCTCATCG GCAAGAGCGC CGTCGCCAGC GTCACCCAGA AAAAGTTCCT CTGCGACCGG

2581 GTCATGTGGC GCATCCCCTT CTCCAGCAAC TTCATGTCCA TGGGCGCGCT CACCGACCTC

2641 GGCCAGAACA TGCTCTACGC CAACTCCGCC CACGCGCTAG ACATGAATTT CGAAGTCGAC

2701 CCCATGGATG AGTCCACCCT TCTCTATGTT GTCTTCGAAG TCTTCGACGT CGTCCGAGTG

2761 CACCAGCCCC ACCGCGGCGT CATCGAGGCC GTCTACCTGC GCACCCCCTT CTCGGCCGGT

2821 AACGCCACCA CCTAA

Fig. 28C

```
   1  ATGGCGACCC CATCGATGAT GCCGCAGTGG TCGTACATGC ACATCTCGGG
CCAGGACGCC

  61  TCNGAGTACC TGAGCCCCGG GCTGGTGCAG TTCGCCCGCG CCACCGAGAG
CTACTTCAGC

 121  CTGAGTAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGG

 181  TCTCAGCGCC TGACGCTGCG GTTCATTCCC GTGGACCGCG AGGACACCGC
GTACTCGTAC

 241  AAGGCGCGGT TCACCCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CTCCACCTAC

 301  TTTGACATCC GCGGGGTGCT GGACCGGGGT CCCACTTTCA AGCCCTACTC
TGGCACCGCC

 361  TACAACTCCC TGGCCCCCAA GGGCGCTCCC AACTCCTGCG AGTGGGAGCA
AGAGGAAACT

 421  CAGGCAGTTG AAGAAGCAGC AGAAGAGGAA GAAGAAGATG CTGACGGTCA
AGCTGAGGAA

 481  GAGCAAGCAG CTACCAAAAA GACTCATGTA TATGCTCAGG CTCCCCTTTC
TGGCGAAAAA

 541  ATTAGTAAAG ATGGTCTGCA AATAGGAACG GACGCTACAG CTACAGAACA
AAAACCTATT

 601  TATGCAGACC CTACATTCCA GCCCGAACCC CAAATCGGGG AGTCACAGTG
GAATGAGGCA

 661  GATGCTACAG TCGCCGGCGG TAGAGTGCTA AAGAAATCTA CTCCCATGAA
ACCATGCTAT

 721  GGTTCCTATG CAAGACCCAC AAATGCTAAT GGAGGTCAGG GTGTACTAAC
GGCAAATGCC

 781  CAGGGACAGC TAGAATCTCA GGTTGAAATG CAATTCTTTT CAACTTCTGA
AAACGCCCGT

 841  AACGAGACTA ACAACATTCA GCCCAAATTG GTGCTGTATA GTGAGGATGT
GCACATGGAG

 901  ACCCCGGATA CGCACCTTTC TTACAAGCCC GCAAAAAGCG ATGACAATTC
AAAAATCATG

 961  CTGGGTCAGC AGTCCATGCC CAACAGACCT AATTACATCG GCTTCAGAGA
TAACTTTATC

1021  GGCCTCATGT ATTACAATAG CACTGGCAAC ATGGGAGTGC TTGCAGGTCA
GGCCTCTCAG

1081  TTGAATGCAG TGGTGGACTT GCAAGACAGA AACACAGAAC TGTCCTACCA
GCTCTTGCTT
```

Fig. 29A

1141 GATTCCATGG GTGACAGAAC CAGATACTTT TCCATGTGGA ATCAGGCAGT
GGACAGTTAT

1201 GACCCAGATG TTAGAATTAT TGAAAATCAT GGAACTGAAG ACGAGCTCCC
CAACTATTGT

1261 TTCCCTCTGG GTGGCATAGG GGTAACTGAC ACTTACCAGG CTGTTAAAAC
CAACAATGGC

1321 AATAACGGGG GCCAGGTGAC TTGGACAAAA GATGAAACTT TTGCAGATCG
CAATGAAATA

1381 GGGGTGGGAA ACAATTTCGC TATGGAGATA AACCTCAGTG CCAACCTGTG
GAGAAACTTC

1441 CTGTACTCCA ACGTGGCGCT GTACCTACCA GACAAGCTTA AGTACAACCC
CTCCAATGTG

1501 GACATCTCTG ACAACCCCAA CACCTACGAT TACATGAACA AGCGAGTGGT
GGCCCCGGGG

1561 CTGGTGGACT GCTACATCAA CCTGGGCGCG CGCTGGTCGC TGGACTACAT
GGACAACGTC

1621 AACCCCTTCA ACCACCACCG CAATGCGGGC CTGCGCTACC GCTCCATGCT
CCTGGGCAAC

1681 GGGCGCTACG TGCCCTTCCA CATCCAGGTG CCCCAGAAGT TCTTTGCCAT
CAAGAACCTC

1741 CTCCTCCTGC CGGGCTCCTA CACCTACGAG TGGAACTTCA GGAAGGATGT
CAACATGGTC

1801 CTCCAGAGCT CTCTGGGTAA CGATCTCAGG GTGGACGGGG CCAGCATCAA
GTTCGAGAGC

1861 ATCTGCCTCT ACGCCACCTT CTTCCCCATG GCCCACAACA CGGCCTCCAC
GCTCGAGGCC

1921 ATGCTCAGGA ACGACACCAA CGACCAGTCC TTCAATGACT ACCTCTCCGC
CGCCAACATG

1981 CTCTACCCCA TACCCGCCAA CGCCACCAAC GTCCCCATCT CCATCCCCTC
GCGCAACTGG

2041 GCGGCCTTCC GCGGCTGGGC CTTCACCCGC CTCAAGACCA AGGAGACCCC
CTCCCTGGGC

2101 TCGGGATTCG ACCCCTACTA CACCTACTCG GGCTCCATTC CCTACCTGGA
CGGCACCTTC

2161 TACCTCAACC ACACTTTCAA GAAGGTCTCG GTCACCTTCG ACTCCTCGGT
CAGCTGGCCG

2221 GGCAACGACC GTCTGCTCAC CCCCAACGAG TTCGAGATCA AGCGCTCGGT
CGACGGGGAG

Fig. 29B

2281 GGCTACAACG TGGCCCAGTG CAACATGACC AAGGACTGGT TCCTGGTCCA
GATGCTGGCC

2341 AACTACAACA TCGGCTACCA GGGCTTCTAC ATCCCAGAGA GCTACAAGGA
CAGGATGTAC

2401 TCCTTCTTCA GGAACTTCCA GCCCATGAGC CGGCAGGTGG TGGACCAGAC
CAAGTACAAG

2461 GACTACCAGG AGGTGGGCAT CATCCACCAG CACAACAACT CGGGCTTCGT
GGGCTACCTC

2521 GCCCCCACCA TGCGCGAGGG ACAGGCCTAC CCCGCCAACT TCCCCTATCC
GCTCATAGGC

2581 AAGACCGCGG TCGACAGCAT CACCCAGAAA AAGTTCCTCT GCGACCGCAC
CCTCTGGCGC

2641 ATCCCCTTCT CCAGCAACTT CATGTCCATG GGTGCGCTCT CGGACCTGGG
CCAGAACTTG

2701 CTCTACGCCA ACTCCGCCCA CGCCCTCGAC ATGACCTTCG AGGTCGACCC
CATGGACGAG

2761 CCCACCCTTC TCTATGTTCT GTTCGAAGTC TTTGACGTGG TCCGGGTCCA
CCAGCCGCAC

2821 CGCGGCGTCA TCGAGACCGT GTACCTGCGT ACGCCCTTCT CGGCCGGCAA
CGCCACCACC

2881 TAA

Fig. 29C

SEQ ID NO: 25

```
   1  ATGGCGACCC CATCGATGAT GCCGCAGTGG TCGTACATGC ACATCTCGGG
CCAGGACGCC

  61  TCGGAGTACC TGAGCCCCGG GCTGGTGCAG TTCGCCCGCG CCACCGAGAG
CTACTTCAGT

 121  CTGAGTAACA AGTTTAGGAA CCCCACGGTG GCGCCCACGC ACGATGTGAC
CACCGACCGG

 181  TCCCAGCGCC TGACGCTGCG GTTCATCCCC GTGGACCGCG AGGACACCGC
GTACTCGTAC

 241  AAGGCGCGGT TCACCCTGGC CGTGGGCGAC AACCGCGTGC TGGACATGGC
CTCCACCTAC

 301  TTTGACATCC GCGGCGTGCT GGACCGCGGC CCCACCTTCA AGCCCTACTC
CGGCACCGCC

 361  TACAACTCCC TGGCCCCCAA GGGCGCTCCC AACTCTTGTG AGTGGGAGCA
ATTAGAAGAA

 421  GCCCAGGCCG CTTTGGAAGA CGAAGAATTA GAAGATGAAG ACGAGGAACC
ACAGGATGAG

 481  GCGCCTGTGA AAAAGACCCA TGTATACGCT CAGGCTCCCC TTTCTGGAGA
AGAAATTACT

 541  AAAGACGGTT TGCAAATAGG GTCAGATAAC ACAGAAGCTC AGTCTAAGCC
TATATATGCA

 601  GACCCTACAT TCCAGCCCGA ACCCCAAATC GGGGAGTCCC AGTGGAACGA
GGCAGATGCT

 661  ACAGTCGCTG GTGGTAGAGT GCTCAAGAAA ACCACTCCCA TGAAACCATG
CTATGGTTCC

 721  TATGCAAGAC CCACGAATGC TAATGGAGGT CAGGGTGTGC TGGTGGCTGA
TGATAAGGGG

 781  GTCCTTCAAT CTAAAGTTGA ATTGCAATTT TTTTCAAATA CTACTACTCT
TAATCAGCGG

 841  GAGGGTAATG ATACAAAACC AAAAGTAGTG CTGTATAGCG AGGATGTGCA
CATGGAAACA

 901  CCAGACACCC ACATTTCTTA CAAGCCCACA AAAAGCGATG ACAATTCTAA
AGTTATGCTG

 961  GGCCAACAGT CCATGCCCAA CAGGCCTAAT TACATCGGCT TCAGAGACAA
CTTTATCGGT

1021  CTCATGTACT ACAACAGCAC TGGCAACATG GGAGTGCTTG CAGGTCAGGC
CTCTCAGTTG

1081  AATGCAGTGG TGGACTTGCA AGACAGAAAC ACAGAACTGT CCTACCAGCT
CTTGCTTGAT
```

Fig. 30A

1141 TCCATGGGTG ACAGAACCAG ATATTTCTCC ATGTGGAATC AGGCAGTGGA
CAGTTATGAC

1201 CCGGATGTCA GAATTATTGA AAATCATGGA ACCGAAGACG AGCTCCCCAA
CTATTGTTTT

1261 CCTCTGGGTG GCATAGGGGT AACTGACACT TACCAGGTCA TTAAAACTAA
TGGCAATGGT

1321 CAAGCAGACC CAACCTGGGA AAAAGATACA GAGTTTGCAG ACCGCAATGA
AATAGGGGTG

1381 GGAAACAATT TCGCCATGGA GATCAACCTC AATGCCAACC TGTGGAGGAA
CTTCCTGTAC

1441 TCCAACGTGG CCCTGTACCT GCCAGACAAG CTTAAGTACA ACCCCTCCAA
CGTGGACATC

1501 TCTGACAACC CCAACACCTA CGATTACATG AACAAGCGAG TGGTGGCCCC
GGGGCTGGTG

1561 GACTGCTACA TCAACCTGGG CGCGCGCTGG TCGCTGGACT ACATGGACAA
CGTCAACCCC

1621 TTCAACCACC ACCGCAACGC GGGCCTGCGC TACCGCTCCA TGCTCCTGGG
CAACGGGCGC

1681 TACGTGCCCT TCCACATCCA GGTGCCCCAG AAGTTCTTTG CCATCAAGAA
CCTCCTCCTC

1741 CTGCCGGGCT CCTACACCTA CGAGTGGAAC TTCAGGAAGG ATGTCAACAT
GGTCCTCCAG

1801 AGCTCTTTGG GCAACGATCT CAGGGTGGAC GGGGCCAGCA TCAAGTTCGA
GAGCATCTGC

1861 CTCTACGCCA CCTTCTTCCC CATGGCCCAC AACACCGCCT CCACGCTCGA
GGCCATGCTC

1921 AGGAACGACA CCAACGACCA GTCCTTCAAT GACTACCTCT CCGCCGCCAA
CATGCTCTAC

1981 CCCATCCCCG CCAACGCCAC CAACGTCCCT ATCTCCATCC CCTCGCGCAA
CTGGGCGGCC

2041 TTCCGCGGCT GGGCCTTCAC CCGCCTCAAG ACCAAGGAGA CACCCTCCCT
GGGCTCGGGA

2101 TTCGACCCCT ACTACACCTA CTCGGGATCC ATTCCCTACC TGGACGGCAC
CTTCTACCTC

2161 AACCACACTT TCAAGAAGGT CTCGGTCACC TTCGACTCCT CGGTCAGCTG
GCCGGGCAAC

2221 GACCGCCTGC TCACCCCCAA CGAGTTCGAG ATCAAGCGCT CGGTCGACGG
GGAGGGCTAC

Fig. 30B

2281 AACGTGGCCC AGTGCAACAT GACCAAGGAC TGGTTCCTGG TCCAGATGCT GGCCAACTAC

2341 AACATCGGCT ACCAGGGCTT CTACATCCCA GAGAGCTACA AGGACAGGAT GTACTCCTTC

2401 TTCAGGAACT TCCAGCCCAT GAGCCGGCAG GTGGTGGACC AAACCAAGTA CAAGGACTAC

2461 CAGGAGGTGG GCATCATCCA CCAGCACAAC AACTCGGGCT TCGTGGGCTA CCTCGCCCCC

2521 ACCATGCGCG AGGGACAGGC CTACCCCGCC AACTTCCCCT ACCCGCTCAT AGGCAAGACC

2581 GCGGTCGACA GCATCACCCA GAAAAAGTTC CTCTGCGACC GCACCCTCTG GCGCATCCCC

2641 TTCTCCAGCA ACTTCATGTC CATGGGTGCG CTCACGGACC TGGGCCAGAA CCTGCTCTAT

2701 GCCAACTCCG CCCACGCGCT CGACATGACC TTCGAGGTCG ACCCCATGGA CGAGCCCACC

2761 CTTCTCTATG TTCTGTTCGA AGTCTTTGAC GTGGTCCGGG TCCACCAGCC GCACCGCGGC

2821 GTCATCGAGA CCGTGTACCT GCGCACGCCC TTCTCGGCCG GCAACGCCAC CACCTAA

Fig. 30C

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          1                                                  50
hAd12  MATPSMMPQW SYMHIAGQDA SEYLSPGLVQ FARATDTYFT LGNKFRNPTV
 hAd3  MATPSMMPQW AYMHIAGQDA SGYLSPGLVQ FARATDTYFS MGNKFRNPTV
 hAd7  MATPSMMPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS MGNKFRNPTV
hAd11  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFN LGNKFRNPTV
hAd21  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFN LGNKFRNPTV
hAd34  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFN LGNKFRNPTV
hAd35  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFN LGNKFRNPTV
   C1  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFN LGNKFRNPTV
 hAd1  MATPSMMPQW SYMHISGQDA SEYLSPGLVQ FARATETYFS LNNKFRNPTV
 hAd2  MATPSMMPQW SYMHISGQDA SEYLSPGLVQ FARATETYFS LNNKFRNPTV
 hAd5  MATPSMMPQW SYMHISGQDA SEYLSPGLVQ FARATETYFS LNNKFRNPTV
ChAd3  MATPSMMPQW SYMHISGQDA SEYLSPGLVQ FARATESYFS LSNKFRNPTV
ChAd11 MATPSMMPQW SYMHISGQDA SEYLSPGLVQ FARATESYFS LSNKFRNPTV
ChAd17 MATPSMMPQW SYMHISGQDA SEYLSPGLVQ FARATESYFS LSNKFRNPTV
ChAd19 MATPSMMPQW SYMHISGQDA SEYLSPGLVQ FARATESYFS LSNKFRNPTV
ChAd20 MATPSMMPQW SYMHISGQDA SEYLSPGLVQ FARATESYFS LSNKFRNPTV
hAd48  MATPSMMPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
ChAd4  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
ChAd5  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
ChAd7  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
ChAd16 MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
 Pan6  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
 hAd4  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
hAd16  MATPSMMPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS MGNKFRNPTV
ChAd6  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
ChAd9  MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
ChAd10 MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
   C68 MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
  Pan5 MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
  Pan7 MATPSMLPQW AYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
hAd41  MATPSMMPQW SYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV
hAd40  MATPSMMPQW SYMHIAGQDA SEYLSPGLVQ FARATDTYFS LGNKFRNPTV

          51                                                 100
hAd12  APTHDVTTDR SQRLTLRFVP VDREDTTYSY KARFTLAVGD NRVLDMASSY
 hAd3  APTHDVTTDR SQRLMLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTF
 hAd7  APTHDVTTDR SQRLMLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTF
hAd11  APTHDVTTDR SQRLMLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTF
hAd21  APTHDVTTDR SQRLMLRFVP VDREDNTYAY KVRYTLAVGD NRVLDMASTF
hAd34  APTHDVTTDR SQRLMLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTF
hAd35  APTHDVTTDR SQRLMLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTF
   C1  APTHDVTTDR SQRLMLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTF
 hAd1  APTHDVTTDR SQRLTLRFIP VDREDTAYSY KARFTLAVGD NRVLDMASTY
 hAd2  APTHDVTTDR SQRLTLRFIP VDREDTAYSY KARFTLAVGD NRVLDMASTY
 hAd5  APTHDVTTDR SQRLTLRFIP VDREDTAYSY KARFTLAVGD NRVLDMASTY
ChAd3  APTHDVTTDR SQRLTLRFIP VDREDTAYSY KARFTLAVGD NRVLDMASTY
ChAd11 APTHDVTTDR SQRLTLRFIP VDREDTAYSY KARFTLAVGD NRVLDMASTY
ChAd17 APTHDVTTDR SQRLTLRFIP VDREDTAYSY KARFTLAVGD NRVLDMASTY
ChAd19 APTHDVTTDR SQRLTLRFIP VDREDTAYSY KARFTLAVGD NRVLDMASTY
ChAd20 APTHDVTTDR SQRLTLRFIP VDREDTAYSY KARFTLAVGD NRVLDMASTY
hAd48  APTHDVTTDR SQRLTLRFVP VDREDTTYSY KARFTLAVGD NRVLDMASTY
ChAd4  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
ChAd5  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
ChAd7  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
ChAd16 APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
```

Fig. 31A

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  Pan6  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
  hAd4  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
 hAd16  APTHDVTTDR SQRLMLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTF
 ChAd6  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
 ChAd9  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
ChAd10  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
   C68  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
  Pan5  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
  Pan7  APTHDVTTDR SQRLTLRFVP VDREDNTYSY KVRYTLAVGD NRVLDMASTY
 hAd41  APTHDVTTDR SQRLTLRFVP VDREDTAYSY KVRFTLAVGD NRVLDMASTY
 hAd40  APTHDVTTDR SQRLTLRFVP VDREETAYSY KVRFTLAVGD NRVLDMASTY

        101                                                  150
 hAd12  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NASQWSD... ..........
  hAd3  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTSQWIVTTN GDNA......
  hAd7  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTSQWIVTAG EERA......
 hAd11  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTSQWIAEGV KNTTGEEHVT
 hAd21  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTSQWIAEGV KKEDGGSDEE
 hAd34  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NASQWLDKGV TSTGLVDDGN
 hAd35  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NASQWIAKGV PTAAAAGNGE
    C1  FDIRGVLDRG PSFKPYSGSA YNSLAPKGAP NTSQWLDKGV TTTDNNTENG
  hAd1  FDIRGVLDRG PTFKPYSGTA YNALAPKGAP NSCEWEQEEP TQEMAEELED
  hAd2  FDIRGVLDRG PTFKPYSGTA YNALAPKGAP NSCEWEQTED SGRAVAEDEE
  hAd5  FDIRGVLDRG PTFKPYSGTA YNALAPKGAP NPCEWDEAAT ALEINLEEED
 ChAd3  FDIRGVLDRG PTFKPYSGTA YNSLAPKGAP NSCEWEQ.EE TQAVEEAAEE
ChAd11  FDIRGVLDRG PTFKPYSGTA YNSLAPKGAP NSCEWEQ.EE TQAVEEAAEE
ChAd17  FDIRGVLDRG PTFKPYSGTA YNSLAPKGAP NSCEWEQ.EE TQAVEEAAEE
ChAd19  FDIRGVLDRG PTFKPYSGTA YNSLAPKGAP NSCEWEQLEE AQAALEDEEL
ChAd20  FDIRGVLDRG PTFKPYSGTA YNSLAPKGAP NPCEWDEAAT ALDIDLNAED
 hAd48  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NPSQWEEKKN GGGS......
 ChAd4  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NSSQWEQKKT GNNA......
 ChAd5  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NSSQWEQKKT GNNA......
 ChAd7  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NSSQWEQKKT GKNA......
ChAd16  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NSSQWEQTEN G.........
  Pan6  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NSSQWEQAKT G.........
  hAd4  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTCQWKD... ..........
 hAd16  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTCQWKD... ..........
 ChAd6  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTSQWITKDN ..........
 ChAd9  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTCQWTYTDN ..........
ChAd10  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTCQWTYTDN ..........
   C68  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTCQWTYKAD GE........
  Pan5  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTCQWTYKAD G.........
  Pan7  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NTCQWTYKAG D.........
 hAd41  FDIRGVLDRG PSFKPYSGTA YNSLAPKTAP NPCEWKD... ..........
 hAd40  FDIRGVLDRG PSFKPYSGTA YNSLAPKGAP NPSQWTN... ..........

        151                                                  200
 hAd12  .......... .......... .NAKLNTFAQ APYLSD...T ITAADGIKVG
  hAd3  .......... .......... VTTTTNTFGI ASMKGG...N ITKE.GLQIG
  hAd7  .......... .......... VTTTTNTFGI ASMKGD...N ITKE.GLEIG
 hAd11  EEE....... .......... TNTTTYTYTFGN APVKAEA..E ITKE.GLPVG
 hAd21  EEK....... .......... .NLTTYTFGN APVKAEG.GD ITKDKGLPIG
 hAd34  DDD....... .......GEE AKKATYTFGN APVKAEA..E ITKD.GLPVG
 hAd35  EEH....... .......ETE EKTATYTFAN APVKAEA..Q ITKE.GLPIG
    C1  DE........ EDEVAEEGEE EKQATYTFGN APVKAEA..E ITKE.GLPIG
  hAd1  EEEAEEEEAE EEAEAPQADQ KVKKTHVYAQ APLAGE...K ITAN.GLQIV
```

Fig. 31B

```
  hAd2  EEE.DEDEEE EEEEQNARDQ ATKKTHVYAQ APLSGE...T ITKS.GLQIG
  hAd5  DDN....EDE VDEQAE.... .QQKTHVFGQ APYSGI...N ITKE.GIQIG
 ChAd3  EE......ED ADGQAEEEQA ATKKTHVYAQ APLSGE...K ISKD.GLQIG
ChAd11  EE......ED ADGQAEEEQA ATKKTHVYAQ APLSGE...K ISKD.GLQIG
ChAd17  EE......ED ADGQAEEEQA ATKKTHVYAQ APLSGE...K ISKD.GLQIG
ChAd19  ED........ .EDEEPQDEA PVKKTHVYAQ APLSGE...E ITKD.GLQIG
ChAd20  DE........ .ESDEAQGEA DQQKTHVFGQ APYSGQ...N ITKE.GIQIG
 hAd48  .......... ........DA NQMQTHTFGV AAMGGI...E ITAK.GLQIG
 ChAd4  .......... .........N GDTENVTYGV AAMGGI...D IDKN.GLQIG
 ChAd5  .......... .........N GDTENVTYGV AAMGGI...D IDKN.GLQIG
 ChAd7  .......... .........N GDTENVTYGV AAMGGI...D IDKN.GLQIG
ChAd16  .......... .......GGQ ATTKTHTYGV APMGGT...N ITVD.GLQIG
  Pan6  .......... ........NG GTMETHTYGV APMGGE...N ITKD.GLQIG
  hAd4  .......... .......... ANSKMHTFGV AAMPGVTGKK IEAD.GLPIR
 hAd16  .......... .......... SDSKMHTFGV AAMPGVTGKK IEAD.GLPIG
 ChAd6  .......... .......... GTDKTYSFGN APVRGL...D ITEE.GLQIG
 ChAd9  .......... .......... QTEKTATYGN APVEGI...N ITKD.GIQLG
ChAd10  .......... .......... QTEKTATYGN APVQGI...S ITKD.GIQLG
   C68  .......... .........T ATEKTYTYGN APVQGI...N ITKD.GIQLG
  Pan5  .......... ........DT GTEKTYTYGN APVQGI...S ITKD.GIQLG
  Pan7  .......... .........T DTEKTYTYGN APVQGI...S ITKD.GIQLG
 hAd41  .......... .......... .NNKIKVRGQ APFIGT...N INKDNGIQIG
 hAd40  .......... .......... .QNKTNSFGQ APYIGQ...K ITNQ.GVQVG

        201                                                  250
 hAd12  TDTAQA...G AAVYANKTYQ PEPQVGPSEW NTSIE.NVKA GGRALKQTTA
  hAd3  KDITTTEGEE KPIYADKTYQ PEPQVGEESW TDTDGTNEKF GGRALKPATN
  hAd7  KDITAD...N KPIYADKTYQ PEPQVGEESW TDTDGTNEKF GGRALKPATK
 hAd11  LEVSDE..ES KPIYADKTYQ PEPQLGDETW TDLDGKTEKY GGRALKPDTK
 hAd21  SEITDG..EA KPIYADKLYQ PEPQVGDETW TDTDGTTEKY GGRALKPETK
 hAd34  LEVSTE..GP KPIYADKLYQ PEPQVGDETW TDLDGKTEEY GGRVLKPETK
 hAd35  LEISAE.NES KPIYADKLYQ PEPQVGDETW TDLDGKTEEY GGRALKPDTK
    C1  LEVPSEG.DP KPIYADKLYQ PEPQVGEESW TDTDGTDEKY GGRALKPETK
  hAd1  SDTQTE...G NPVFADPTYQ PEPQVGESQW NEAEA..TAS GGRVLKKTTP
  hAd2  SDNAET..QA KPVYADPSYQ PEPQIGESQW NEADA..NAA GGRVLKKTTP
  hAd5  VEGQ...... TPKYADKTFQ PEPQIGESQW YETEI..NHA AGRVLKKTTP
 ChAd3  TDATAT..EQ KPIYADPTFQ PEPQIGESQW NEADA..TVA GGRVLKKSTP
ChAd11  TDATAT..EQ KPIYADPTFQ PEPQIGESQW NEADA..TVA GGRVLKKTTP
ChAd17  TDATAT..EQ KPIYADPTFQ PEPQIGESQW NEADA..TVA GGRVLKKSTP
ChAd19  SDNTEA..QS KPIYADPTFQ PEPQIGESQW NEADA..TVA GGRVLKKTTP
ChAd20  IDAASQ..AQ TPVYADKTFQ PEPQVGESQW NETEI..SYG AGRVLKKTTL
 hAd48  IDATKEEDNG KEIYADKTFQ PEPQIGEENW QDSD...NYY GGRAIKKETK
 ChAd4  TDDTKD..DD NEIYADKTYQ PEPQIGEENW QETY...SYY GGRALKKDTK
 ChAd5  TDDTKD..DD NEIYADKTYQ PEPQIGEENW QETY...SYY GGRALKKDTK
 ChAd7  TDDTKD..GD NEIYADKTYQ PEPQIGEENW QETY...SYY GGRALKKDTK
ChAd16  TDATAD..TE KPIYADKTFQ PEPQIGEENW QETE...SFY GGRALKKDTN
  Pan6  TDVTAN..QN KPIYADKTFQ PEPQVGEENW QETE...NFY GGRALKKDTN
  hAd4  IDSTSG..TD TVIYADKTFQ PEPQVGNDSW VDTNDAEEKY GGRALKDTTN
 hAd16  IDSTSG..TD TVIYADKTFQ PEPQVGNASW VDANGTEEKY GGRALKDTTK
 ChAd6  PDESGG..ES KKIFADKTYQ PEPQLGDEEW HDTIGAEDKY GGRALKPATN
 ChAd9  TDSDG..... QAIYADETYQ PEPQVGDPEW HDTTGTEEKY GGRALKPATD
ChAd10  TDTDD..... QPIYADKTYQ PEPQVGDAEW HDITGTDEKY GGRALKPDTK
   C68  TDTDD..... QPIYADKTYQ PEPQVGDAEW HDITGTDEKY GGRALKPDTK
  Pan5  TDTDD..... QPIYADKTYQ PEPQVGDAEW HDITGTDEKY GGRALKPDTK
  Pan7  TDSDG..... QAIYADETYQ PEPQVGDAEW HDITGTDEKY GGRALKPDTK
 hAd41  TDTTN..... QPIYADKTYQ PEPQVGQTQW NSEVGAAQKV AGRVLKDTTP
 hAd40  SDSNN..... RDVFADKTYQ PEPQVGQTQW NINPM..QNA AGRILKQTTP
```

Fig. 31C

```
          251                                                        300
hAd12   MQPCYGSYAR PTNEHGGQS. .......... ....KDDNIE LKFFDSANNA
 hAd3   MKPCYGSFAR PTNIKGGQAK NRKVKPTTEG GVETEEPDID MEFFDGRDAV
 hAd7   MKPCYGSFAR PTNIKGGQAK NRKVKP.TEG DVETEEPDID MEFFDGREAA
hAd11   MKPCYGSFAK PTNVKGGQAK QKTTEQPN.. ..QKVEYDID MEFFDAASQK
hAd21   MKPCYGSFAK PTNVKGGQAK QKTTEQPQ.. .NQQVEYDID MNFFDEASQK
hAd34   MKPCYGSFAK PTNIKGGQAK VKPKEDDG.. .TNNIEYDID MNFFDLRSQR
hAd35   MKPCYGSFAK PTNVKGGQAK QKTTEQP... .NQKVEYDID MEFFDAASQR
   C1   MKPCYGSFAK PTNVKGGQAK VKKVEEG... ...KVEYDID MNFFDLRSQK
 hAd1   MKPCYGSYAR PTNKNGGQGI LVANNQG... ...ALESKVE MQFFAPSGTA
 hAd2   MKPCYGSYAR PTNPFGGQSV LVPDEKG... ...VPLPKVD LQFFSNTTSL
 hAd5   MKPCYGSYAK PTNENGGQGI LVKQQNG... ...KLESQVE MQFFSTTEAT
ChAd3   MKPCYGSYAR PTNANGGQGV LTANAQG... ...QLESQVE MQFFSTSENA
ChAd11  MKPCYGSYAR PTNANGGQGV LAANAQG... ...QLESQVE MQFFSTSENA
ChAd17  MKPCYGSYAR PTNANGGQGV LTANAQG... ...QLESQVE MQFFSTSENA
ChAd19  MKPCYGSYAR PTNANGGQGV LVADDKG... ...VLQSKVE LQFFSNTTTL
ChAd20  MKPCYGSYAR PTNENGGQGI LLEQDG.... ...KKESQVE MQFFSTTQAA
hAd48   MKPCYGSFAR PTNEKGGQAK FKTPEKEGE. ..EPKELDID LNFFDIPSTG
ChAd4   MKPCYGSFAR PTNVKGGQAK IKTDGD.... ...VKSFDID LAFFDIPNSG
ChAd5   MKPCYGSFAR PTNVKGGQAK IKTDGD.... ...VKSFDID LAFFDIPNSG
ChAd7   MKPCYGSFAR PTNVKGGQAK IKTDGD.... ...VKSFDID LAFFDIPNSG
ChAd16  MKPCYGSFAR PTNEKGGQAK LKVGADG... .LPTKEFDID LAFFDTPGGT
 Pan6   MKPCYGSYAR PTNEKGGQAK LKVGDDG... .VPTKEFDID LAFFDTPGGT
 hAd4   MNPCYGSFAK PTNKEGGQAN LKDSETA... .ATTPNYDID LAFFDGKNIV
hAd16   MKPCYGSFAK PTNKEGGQAN LKDSETA... .ATTPNYDID LAFFDNKNIA
ChAd6   MKPCYGSFAK PTNAKGGQAK SRTKDDG... ...TTEPDID MAFFDDRSQQ
ChAd9   MKPCYGSFAK PTNVKGGQAK SRTKTDG... ...TTEPDID MAFFDGRNAT
ChAd10  MKPCYGSFAK PTNKEGGQAN VKTETGG... ...TKEYDID MAFFDNRSAA
   C68  MKPCYGSFAK PTNKEGGQAN VKTGTGT... ...TKEYDID MAFFDNRSAA
 Pan5   MKPCYGSFAK PTNKEGGQAN VKTETGG... ...TKEYDID MAFFDNRSAA
 Pan7   MKPCYGSFAK PTNKEGGQAN VKTETGG... ...TKEYDID MAFFDNRSAA
hAd41   MLPCYGSYAK PTNEKGGQAS LITNGTD... ..QTLTSDVN LQFFALPST.
hAd40   MQPCYGSYAR PTNEKGGQAK LVKNDDN... ..QTTTTNVG LNFFTTATET

          301                                                        350
hAd12   A........N TAQVVFYTED VNLEMPDTHL VFKPTVTNGT IASESLLGQQ
 hAd3   A......GAL APEIVLYTEN VNLETPDSHV VYKPETSNN. ..SHANLGQQ
 hAd7   D.......AF SPEIVLYTEN VNLETPDSHV VYKPGTSDDN ..SHANLGQQ
hAd11   T.......NL SPKIVMYAEN VNLETPDTHV VYKPGTEDTS ..SEANLGQQ
hAd21   A.......NF SPKIVMYAEN VDLETPDTHV VYKPGTSEES ..SHANLGQQ
hAd34   S.......EL KPKIVMYAEN VDLESPDTHV VYKPGVSDAS ..SETNLGQQ
hAd35   T.......NF SPKIVMYAEN VGLETPDTHV VYKPGTEDTS ..SEANLGQQ
   C1   .......TGL KPKIVMYAEN VDLETPDTHV VYKPGASDAS ..SHANLGQQ
 hAd1   MN...ERNAV QPSIVLYSED VNMETPDTHI SYKPSKTDEN ..SKAMLGQQ
 hAd2   NDR..QGNAT KPKVVLYSED VNLETPDTHL SYKPGKGDEN ..SKAMLGQQ
 hAd5   AG...NGDNL TPKVVLYSED VDIETPDTHI SYMPTIKEGN ..SRELMGQQ
ChAd3   RN...EANNI QPKLVLYSED VHMETPDTHL SYKPAKSDDN ..SKIMLGQQ
ChAd11  RN...EANNI QPKLVLYSED VHMETPDTHL SYKPTKSDDN ..SKVMLGQQ
ChAd17  RN...ETNNI QPKLVLYSED VHMETPDTHL SYKPAKSDDN ..SKIMLGQQ
ChAd19  NQR..EGNDT KPKVVLYSED VHMETPDTHI SYKPTKSDDN ..SKVMLGQQ
ChAd20  AG...NSDNP TPKVVLYSED VNLETPDTHI SYMPTNNETN ..SRELLGQQ
hAd48   TGGNGTNVNF KPDMIMYAEN VNLETPDTHI VYKPGKEDAS ..SESNLTQQ
ChAd4   AGNG.TNVND DPDMVMYTEN VNLETPDTHI VYKPGTSDDS ..SKVNLCQQ
ChAd5   AGNG.TNVND DPDMVMYTEN VNLETPDTHI VYKPGTSDDS ..SKVNLCQQ
```

Fig. 31D

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ChAd7   AGNG.TNVND DPDMVMYTEN VNLETPDTHI VYKPGTSDDS ..SEVNLCQQ
ChAd16  VTG..GTEEY KADIVMYTEN TYLETPDTHV VYKPGKDNTS ..SKINLVQQ
Pan6    VN...GQDEY KADIVMYTEN TYLETPDTHV VYKPGKDDAS ..SEINLVQQ
hAd4    A.......NY DPDIVMYTEN VDLQTPDTHI VYKPGKEDTS ..SESNLGQQ
hAd16   A.......NY DPDIVMYTEN VDLQTPDTHI VYKPGTEDTS ..SESNLGQQ
ChAd6   A.......SF SPELVLYTEN VDLDTPDTHI IYKPGTDETS ..SSFNLGQQ
ChAd9   T......AGL TPEIVLYTEN VDLETPDTHI VYKAGTDDSS ..SSINLGQQ
ChAd10  A......AGL APEIVLYTEN VDLETPDTHI VYKAGTDDSS ..SSINLGQQ
C68     A......AGL APEIVLYTEN VDLETPDTHI VYKAGTDDSS ..SSINLGQQ
Pan5    AA......GL APEIVLYTEN VDLETPDTHI VYKAGTDDSS ..SSINLGQQ
Pan7    AA......GL APEIVLYTEN VDLETPDTHI VYKAGTDDSS ..SSINLGQQ
hAd41   ........PN EPKAVLYAEN VSIEAPDTHL VYKPDVAQGT ISSADLLTQQ
hAd40   A.......NF SPKVVLYSED VNLEAPDTHL VFKPDVNGTS ..AELLLGQQ

        351                                                  400
hAd12   AAPNRANYIA FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd3    AMPNRPNYIG FRDNFVGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd7    AMPNRPNYIG FRDNFVGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd11   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd21   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd34   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd35   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
C1      SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd1    AMPNRPNYIA FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd2    SMPNRPNYIA FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd5    SMPNRPNYIA FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd3   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd11  AMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd17  SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd19  SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd20  AMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd48   SMPNRPNYIG FRDNFVGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd4   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd5   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd7   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd16  SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
Pan6    SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd4    AMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd16   AMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd6   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd9   SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
ChAd10  SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
C68     AMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
Pan5    SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
Pan7    SMPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd41   AAPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL
hAd40   AAPNRPNYIG FRDNFIGLMY YNSTGNMGVL AGQASQLNAV VDLQDRNTEL

        401                                                  450
hAd12   SYQLMLDALG DRTRYFSLWN SAVDSYDPDV RVIENHGVED ELPNYCFPLS
hAd3    SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGIED ELPNYCFPLN
hAd7    SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGIED ELPNYCFPLD
hAd11   SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RVIENHGVED ELPNYCFPLD
hAd21   SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
hAd34   SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RVIENHGVED ELPNYCFPLD
hAd35   SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RVIENHGVED ELPNYCFPLN
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Fig. 31E

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    C1  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RVIENHGVED ELPNYCFPLD
  hAd1  SYQLLLDSIG DRTRYFSMWN QAVDSYDPDV RIIENHGTED ELPNYCFPLG
  hAd2  SYQLLLDSIG DRTRYFSMWN QAVDSYDPDV RIIENHGTED ELPNYCFPLG
  hAd5  SYQLLLDSIG DRTRYFSMWN QAVDSYDPDV RIIENHGTED ELPNYCFPLG
 ChAd3  SYQLLLDSMG DRTRYFSMWN QAVDSYDPDV RIIENHGTED ELPNYCFPLG
ChAd11  SYQLLLDSMG DRTRYFSMWN QAVDSYDPDV RIIENHGTED ELPNYCFPLG
ChAd17  SYQLLLDSMG DRTRYFSMWN QAVDSYDPDV RIIENHGTED ELPNYCFPLG
ChAd19  SYQLLLDSMG DRTRYFSMWN QAVDSYDPDV RIIENHGTED ELPNYCFPLG
ChAd20  SYQLLLDSMG DRTRYFSMWN QAVDSYDPDV RIIENHGTED ELPNYCFPLG
 hAd48  SYQLLLDSLG DRTRYFSMWN SAVDSYDPDV RIIENHGVED ELPNYCFPLD
 ChAd4  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
 ChAd5  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
 ChAd7  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
ChAd16  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
  Pan6  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
  hAd4  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLN
 hAd16  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLN
 ChAd6  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLN
 ChAd9  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLN
ChAd10  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLN
    C68  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
  Pan5  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
  Pan7  SYQLLLDSLG DRTRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLD
 hAd41  SYQLMLDALG DRSRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLG
 hAd40  SYQLMLDALG DRSRYFSMWN QAVDSYDPDV RIIENHGVED ELPNYCFPLN

        451                                                 500
 hAd12  AVG.EIKNYK GIKPDNG... ..GGGGWTAD N.TVSEANHI GIGNIAAMEI
  hAd3  GIG.PGHTYQ GIKVKTD... ..DTNGWEKD A.NVAPANEI TIGNNLAMEI
  hAd7  GIG.PAKTYQ GIKSK..... ...DNGWEKD D.NVSKSNEI AIGNNQAMEI
 hAd11  GIGVPTTSYK SIVPNGD... ..NAPNWKEP ..EVNGTSEI GQGNLFAMEI
 hAd21  GVGVPISSYK IIEPNG.... ..QGADWKEP ..DINGTSEI GQGNLFAMEI
 hAd34  GVGPQTDSYK EIKPNG.... ..DQSTWTNV ..DPNGSSQL AKGNPFAMEI
 hAd35  GIGVPTTSYK SIVPNGE... ..DNNNWKEP ..EVNGTSEI GQGNLSAMEI
    C1  GVGPRTDSYK GIETNGD... ...ENTTWKD L.DPNGISEL AKGNPFAMEI
  hAd1  GIG.VTDTYQ GIKSNGNG.. ..NPQNWTKN D.DFAARNEI GVGNNFALEI
  hAd2  GIG.VTDTYQ AIKANGNGAG DNGNTTWTKD E.TFATRNEI GVGNNFAMEI
  hAd5  GVI.NTETLT KVKPKTG... ..QENGWEKD ATEFSDKNEI RVGNNFAMEI
 ChAd3  GIG.VTDTYQ AVKTNNGNNG ..GQVTWTKD E.TFADRNEI GVGNNFAMEI
ChAd11  GIG.VTDTYQ AVKTNNGNNG ..GQVTWTKD E.TFAERNEI GVGNNFAMEI
ChAd17  GIG.VTDTYQ AVKTNNGNNG ..GQVTWTKD E.TFADRNEI GVGNNFAMEI
ChAd19  GIG.VTDTYQ VIKT.NGNGQ ..ADPTWEKD T.EFADRNEI GVGNNFAMEI
ChAd20  GVI.NTETFT KVKPKAAQ.. ...DAQWEKD S.EFSDKNEI RVGNNFAMEI
 hAd48  GAG.TNAVYQ GVKVKTT... ..NNTEWEKD T.AVSEHNQI CKGNVYAMEI
 ChAd4  GAG.TNSVYQ GVKPKTDN.. ..GNDQWETD S.TVSSHNQI CKGNIYAMEI
 ChAd5  GAG.TNSVYQ GVKPKTDN.. ..GNDQWETD S.TVSSHNQI CKGNIYAMEI
 ChAd7  GAG.TNSVYQ GVKPKTDN.. ..GNDQWETD S.TVSSHNQI CKGNIYAMEI
ChAd16  GSG.TNAAYQ GVKVKNGQDG .DVESEWEKD D.TVAARNQL CKGNIFAMEI
  Pan6  GSG.TNAAYQ GVKVKDGQDG .DVESEWEND D.TVAARNQL CKGNIFAMEI
  hAd4  GVG.LTDTYQ GVKVKTDA.. ..GSEKWDKD DTTVSTANEI HVGNPFAMEI
 hAd16  GVG.FTDTYQ GVKVKTDAVA GTSGTQWDKD DTTVSTANEI HGGNPFAMEI
 ChAd6  GVG.FTDTFQ GIKVKTTNNG TANATEWESD T.SVNNANEI AKGNPFAMEI
 ChAd9  AVG.RTNSYQ GIKPNGG... ..DPATWAKD E.SVNDSNEL GKGNPFAMEI
ChAd10  AVG.RTDTYQ GIKANGA... ..DQTTWTKD D.TVNDANEL GKGNPFAMEI
    C68  AVG.RTDTYQ GIKANGT... ..DQTTWTKD D.SVNDANEI GKGNPFAMEI
  Pan5  AVG.RTDTYQ GIKANGA... ..DQTTWTKD D.TVNDANEL GKGNPFAMEI
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Fig. 31F

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  Pan7  AVG.RTDTYQ GIKANGD... ..NQTTWTKD D.TVNDANEL GKGNPFAMEI
 hAd41  GSA.ATDTYS GIKAN..... ...GQTWTAD DNYADRGAEI ESGNIFAMEI
 hAd40  GQG.ISNSYQ GVKTDN.... ...GTNWSQN NTDVSSNNEI SIGNVFAMEI

        501                                                  550
 hAd12  NLQANLWRSF LYSNVGLYLP DDLKYTPGNI KLPDNKNTYE YMNGRVTAPG
  hAd3  NIQANLWRSF LYSNVALYLP DVYKYTPPNI TLPTNTNTYE YMNGRVVSPS
  hAd7  NIQANLWRSF LYSNVALYLP DVYKYTPTNI TLPANTNTYE YMNGRVVSPS
 hAd11  NLQANLWRSF LYSNVALYLP DSYKYTPSNV TLPENKNTYD YMNGRVVPPS
 hAd21  NLQANLWRSF LYSNVALYLP DSYKYTPANV TLPTNNNTYD YMNGRVVPPS
 hAd34  NLQANLWRSF LYSNVALYLP DSYKYTPSNV TLPENKNTYD YMNGRVVPPS
 hAd35  NLQANLWRSF LYSNVALYLP DSYKYTPSNV TLPENKNTYD YMNGRVVPPS
    C1  NIQANLWRSF LYSNVALYLP DSYKYTPTNV TLPENKNTYD YMNGRVVPPS
  hAd1  NLNANLWRNF LYSNIALYLP DKLKYTPTNV EISPNPNSYD YMNKRVVAPG
  hAd2  NLNANLWRNF LYSNIALYLP DKLKYNPTNV EISDNPNTYD YMNKRVVAPG
  hAd5  NLNANLWRNF LYSNIALYLP DKLKYSPSNV KISDNPNTYD YMNKRVVAPG
 ChAd3  NLSANLWRNF LYSNVALYLP DKLKYNPSNV DISDNPNTYD YMNKRVVAPG
ChAd11  NLNANLWRNF LYSNVALYLP DKLKYNPSNV DISDNPNTYD YMNKRVVAPG
ChAd17  NLSANLWRNF LYSNVALYLP DKLKYNPSNV DISDNPNTYD YMNKRVVAPG
ChAd19  NLNANLWRNF LYSNVALYLP DKLKYNPSNV DISDNPNTYD YMNKRVVAPG
ChAd20  NLNANLWRNF LYSNVALYLP DKLKYTPSNV QISNNPNSYD YMNKRVVAPG
 hAd48  NLQANLWKSF LYSNVALYLP DSYKYTPANV TLPTNTNTYE YMNGRVVAPS
 ChAd4  NLQANLWRSF LYSNVALYLP DSYKYTPANI TLPTNTNTYD YMNGRVVPPS
 ChAd5  NLQANLWRSF LYSNVALYLP DSYKYTPANI TLPTNTNTYD YMNGRVVPPS
 ChAd7  NLQANLWRSF LYSNVALYLP DSYKYTPANI TLPTNTNTYD YMNGRVVPPS
ChAd16  NLQANLWRSF LYSNVALYLP DSYKYTPANI TLPTNTNTYD YMNGRVVPPS
  Pan6  NLQANLWRSF LYSNVALYLP DSYKYTPTNV TLPTNTNTYD YMNGRVTPPS
  hAd4  NIQANLWRNF LYANVALYLP DKYKYTPANI TLPTNTNTYE YMNGRVVAPS
 hAd16  NIQANLWRSF LYSNVALYLP DSYKYTPSNV TLPENKNTYD YMNGRVVPPS
 ChAd6  NIQANLWRNF LYANVALYLP DSYKYTPANI TLPANTNTYD YMNGRVVAPS
 ChAd9  NIQANLWRNF LYANVALYLP DSYKYTPANI TLPANTNTYD YMNGRVVAPS
ChAd10  NIQANLWRNF LYANVALYLP DSYKYTPANI TLPTNTNTYD YMNGRVVAPS
   C68  NIQANLWRNF LYANVALYLP DSYKYTPANV TLPTNTNTYD YMNGRVVAPS
  Pan5  NIQANLWRNF LYANVALYLP DSYKYTPANI TLPTNTNTYD YMNGRVVAPS
  Pan7  NIQANLWRNF LYANVALYLP DSYKYTPANI TLPTNTNTYD YMNGRVVAPS
 hAd41  NLAANLWRSF LYSNVALYLP DSYKITPDNI TLPENKNTYA YMNGRVAVPS
 hAd40  NLAANLWRSF LYSNVALYLP DSYKITPDNI TLPDNKNTYA YMNGRVAVPS

        551                                                  600
 hAd12  LVDTYVNIGA RWSPDVMDNV NPFNHHRNAG LRYRSMLLGN GRFVPFHIQV
  hAd3  LVDSYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
  hAd7  LVDSYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd11  LVDTYVNIGA RWSLDAMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd21  LVDTYVNIGA RWSLDAMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd34  LVDTYVNIGA RWSLDAMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd35  LVDTYVNIGA RWSLDAMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
    C1  LVDTYVNIGA RWSLDAMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
  hAd1  LVDCYINLGA RWSLDYMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
  hAd2  LVDCYINLGA RWSLDYMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
  hAd5  LVDCYINLGA RWSLDYMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 ChAd3  LVDCYINLGA RWSLDYMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
ChAd11  LVDCYINLGA RWSLDYMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
ChAd17  LVDCYINLGA RWSLDYMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
ChAd19  LVDCYINLGA RWSLDYMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
ChAd20  LVDCYINLGA RWSLDYMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd48  LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
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Fig. 31G

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ChAd4   LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
ChAd5   LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
ChAd7   LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
ChAd16  LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 Pan6   LVDAYLNIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd4   LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd16  LVDTYVNIGA RWSLDAMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 ChAd6  LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 ChAd9  LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
ChAd10  LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
  C68   LVDSYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 Pan5   LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 Pan7   LVDAYINIGA RWSLDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd41  ALDTYVNIGA RWSPDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV
 hAd40  ALDTYVNIGA RWSPDPMDNV NPFNHHRNAG LRYRSMLLGN GRYVPFHIQV

        601                                                  650
 hAd12  PQKFFAIRNL LLLPGSYTYE WNFRKDVNMI LQSTLGNDLR VDGASVRFDN
  hAd3  PQKFFAVKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR TDGATISFTS
  hAd7  PQKFFAVKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR TDGATISFTS
 hAd11  PQKFFAVKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASISFTS
 hAd21  PQKFFAVKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASISFTS
 hAd34  PQKFFAVKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASISFTS
 hAd35  PQKFFAVKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASISFTS
   C1   PQKFFAVKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASISFTS
  hAd1  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASIKFDS
  hAd2  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASIKFDS
  hAd5  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASIKFDS
 ChAd3  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASIKFES
ChAd11  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASIKFES
ChAd17  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASIKFES
ChAd19  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASIKFES
ChAd20  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR VDGASIKFES
 hAd48  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR VDGASVRFDS
 ChAd4  PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASISFTS
 ChAd5  PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASISFTS
 ChAd7  PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASISFTS
ChAd16  PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASISFTS
 Pan6   PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASIAFTS
 hAd4   PQKFFAIKNL LLLPGSYTYE WNFRKDVNMV LQSSLGNDLR TDGASITFTS
 hAd16  PQKFFAVKNL LLLPGSYTYV WNFRKDVNMV LQSSLGNDLR VDGATISFTS
 ChAd6  PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASIAFTS
 ChAd9  PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASIAFTS
ChAd10  PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASIAFTS
  C68   PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASISFTS
 Pan5   PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASIAFTS
 Pan7   PQKFFAIKSL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR TDGASIAFTS
 hAd41  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR VDGASVRFDS
 hAd40  PQKFFAIKNL LLLPGSYTYE WNFRKDVNMI LQSSLGNDLR VDGASVRFDS

        651                                                  700
 hAd12  IALYANFFPM AHNTASTLEA MLRNDTNDQS FNDYLCAANM LYPIPANATS
  hAd3  INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
  hAd7  INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 hAd11  INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 hAd21  INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
```

Fig. 31H

```
hAd34   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
hAd35   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
  C1    INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 hAd1   ICLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 hAd2   ICLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 hAd5   ICLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd3   ICLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd11  ICLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd17  ICLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd19  ICLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd20  ICLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 hAd48  VNLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPAKATN
ChAd4   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd5   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd7   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd16  INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 Pan6   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 hAd4   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
hAd16   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd6   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd9   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
ChAd10  INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
  C68   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 Pan5   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
 Pan7   INLYATFFPM AHNTASTLEA MLRNDTNDQS FNDYLSAANM LYPIPANATN
hAd41   INLYANFFPM AHNTASTLEA MLRNDTNDQS FNDYLCAANM LYPIPSNATS
hAd40   INLYANFFPM AHNTASTLEA MLRNDTNDQS FNDYLCAANM LYPIPANATS

        701                                                 750
hAd12   VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GTIPYLDGTF
 hAd3   IPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
 hAd7   IPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
hAd11   IPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
hAd21   VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
hAd34   IPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
hAd35   IPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
  C1    VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
 hAd1   VPISIPSRNW AAFRGWAFTR LKTKETPSLG SGYDPYYTYS GSIPYLDGTF
 hAd2   VPISIPSRNW AAFRGWAFTR LKTKETPSLG SGYDPYYTYS GSIPYLDGTF
 hAd5   VPISIPSRNW AAFRGWAFTR LKTKETPSLG SGYDPYYTYS GSIPYLDGTF
ChAd3   VPISIPSRNW AAFRGWAFTR LKTKETPSLG SGFDPYYTYS GSIPYLDGTF
ChAd11  VPISIPSRNW AAFRGWAFTR LKTKETPSLG SGFDPYYTYS GSIPYLDGTF
ChAd17  VPISIPSRNW AAFRGWAFTR LKTKETPSLG SGFDPYYTYS GSIPYLDGTF
ChAd19  VPISIPSRNW AAFRGWAFTR LKTKETPSLG SGFDPYYTYS GSIPYLDGTF
ChAd20  VPISIPSRNW AAFRGWAFTR LKTKETPSLG SGFDPYYTYS GSIPYLDGTF
 hAd48  VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
ChAd4   VPISIPSRNW AAFRGWSFTR LKTRETPSLG SGFDPYFVYS GSIPYLDGTF
ChAd5   VPISIPSRNW AAFRGWSFTR LKTRETPSLG SGFDPYFVYS GSIPYLDGTF
ChAd7   VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
ChAd16  VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
 Pan6   VPISIPSRNW AAFRGWSFTR LKTRETPSLG SGFDPYFVYS GSIPYLDGTF
 hAd4   VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
hAd16   IPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
ChAd6   VPISIPSRNW AAFRGWSFTR LKTRETPSLG SGFDPYFVYS GSIPYLDGTF
ChAd9   VPISIPSRNW AAFRGWSFTR LKTRETPSLG SGFDPYFVYS GSIPYLDGTF
ChAd10  VPISIPSRNW AAFRGWSFTR LKTRETPSLG SGFDPYFVYS GSIPYLDGTF
```

Fig. 31I

```
C68     VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFVYS GSIPYLDGTF
Pan5    VPISIPSRNW AAFRGWSFTR LKTRETPSLG SGFDPYFVYS GSIPYLDGTF
Pan7    VPISIPSRNW AAFRGWSFTR LKTRETPSLG SGFDPYFVYS GSIPYLDGTF
hAd41   VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFTYS GSVPYLDGTF
hAd40   VPISIPSRNW AAFRGWSFTR LKTKETPSLG SGFDPYFTYS GSVPYLDGTF

        751                                                  800
hAd12   YLNHTFKKVS IMFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
hAd3    YLNHTFKKVA IMFDSSVSWP GNDRLLSPNE FEIKRTVDGE GYNVAQCNMT
hAd7    YLNHTFKKVS IMFDSSVSWP GNDRLLSPNE FEIKRTVDGE GYNVAQCNMT
hAd11   YLNHTFKKVS IMFDSSVSWP GNDRLLSPNE FEIKRTVDGE GYNVAQCNMT
hAd21   YLNHTFKKVS IMFDSSVSWP GNDRLLSPNE FEIKRTVDGE GYNVAQCNMT
hAd34   YLNHTFKKVS IMFDSSVSWP GNDRLLSPNE FEIKRTVDGE GYNVNQCNMT
hAd35   YLNHTFKKVS IMFDSSVSWP GNDRLLSPNE FEIKRTVDGE GYNVAQCNMT
C1      YLNHTFKKVS IMFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
hAd1    YLNHTFKKVA ITFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
hAd2    YLNHTFKKVA ITFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
hAd5    YLNHTFKKVA ITFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
ChAd3   YLNHTFKKVS VTFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
ChAd11  YLNHTFKKVS VTFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
ChAd17  YLNHTFKKVS VTFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
ChAd19  YLNHTFKKVS VTFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
ChAd20  YLNHTFKKVS VTFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
hAd48   YLNHTFKKVS IMFDSSVSWP GNDRLLTPNE FEIKRSVDGE GYNVAQCNMT
ChAd4   YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
ChAd5   YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
ChAd7   YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
ChAd16  YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
Pan6    YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
hAd4    YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
hAd16   YLNHTFKKVS IMFDSSVSWP GNDRLLSPNE FEIKRTVDGE GYNVAQCNMT
ChAd6   YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
ChAd9   YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
ChAd10  YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
C68     YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
Pan5    YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
Pan7    YLNHTFKKVS ITFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
hAd41   YLNHTFKKVS IMFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT
hAd40   YLNHTFKKVS VMFDSSVSWP GNDRLLTPNE FEIKRTVDGE GYNVAQCNMT

        801                                                  850
hAd12   KDWFLIQMLS HYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDTTEYK
hAd3    KDWFLVQMLA NYNIGYQGFY IPEGYKDRMY SFFRNFQPMS RQVVDEVNYT
hAd7    KDWFLVQMLA NYNIGYQGFY IPEGYKDRMY SFFRNFQPMS RQVVDEVNYT
hAd11   KDWFLVQMLA NYNIGYQGFY IPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
hAd21   KDWFLVQMLA NYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEINYK
hAd34   KDWFLVQMLA NYNIGYQGFY IPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
hAd35   KDWFLVQMLA NYNIGYQGFY IPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
C1      KDWFLVQMLA NYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEINYK
hAd1    KDWFLVQMLA NYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDDTKYK
hAd2    KDWFLVQMLA NYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDDTKYK
hAd5    KDWFLVQMLA NYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDDTKYK
ChAd3   KDWFLVQMLA NYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDQTKYK
ChAd11  KDWFLVQMLA NYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDQTKYK
ChAd17  KDWFLVQMLA NYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDQTKYK
ChAd19  KDWFLVQMLA NYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDQTKYK
```

Fig. 31J

```
ChAd20  KDWFLVQMLA NYNIGYQGFY IPESYKDRMY SFFRNFQPMS RQVVDQTKYK
 hAd48  KDWFLVQMLS HYNIGYQGFH VPEGYKDRMY SFFRNFQPMS RQVVDEINYK
 ChAd4  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
 ChAd5  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
 ChAd7  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
ChAd16  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
  Pan6  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
  hAd4  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
 hAd16  KDWFLVQMLA NYNIGYQGFY IPEGYKDRMY SFFRNFQPMS RQVVDEVNYT
 ChAd6  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
 ChAd9  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
ChAd10  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
   C68  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
  Pan5  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
  Pan7  KDWFLVQMLA HYNIGYQGFY VPEGYKDRMY SFFRNFQPMS RQVVDEVNYK
 hAd41  KDWFLIQMLS HYNIGYQGFY VPESYKDRMY SFFRNFQPMS RQVVNTTTYK
 hAd40  KDWFLIQMLS HYNIGYQGFH VPESYKDRMY SFFRNFQPMS RQVVDTTTYT

        851                                                 900
 hAd12  NYKKVTVEFQ HNNSGFVGYL GPTMREGQAY PANYPYPLIG QTAVESITQK
  hAd3  DYKAVTLPYQ HNNSGFVGYL APTMRQGEPY PANYPYPLIG TTAVKSVTQK
  hAd7  DYKAVTLPYQ HNNSGFVGYL APTMRQGEPY PANYPYPLIG TTAVKSVTQK
 hAd11  DFKAVAIPYQ HNNSGFVGYM APTMRQGQPY PANYPYPLIG TTAVNSVTQK
 hAd21  DYKAVAVPYQ HNNSGFVGYM APTMRQGQAY PANYPYPLIG TTAVTSVTQK
 hAd34  DFKAVAIPYQ HNNSGFVGYM APTMRQGQPY PANYPYPLIG TTAVNSVTQK
 hAd35  DFKAVAIPYQ HNNSGFVGYM APTMRQGQPY PANYPYPLIG TTAVNSVTQK
    C1  DYKAVAVPYQ HNNSGFVGYM APTMRQGQAY PANYPYPLIG TTAVTSVTQK
  hAd1  DYQQVGILHQ HNNSGFVGYL APTMREGQAY PANFPYPLIG KTAVDSITQK
  hAd2  DYQQVGIIHQ HNNSGFVGYL APTMREGQAY PANVPYPLIG KTAVDSITQK
  hAd5  DYQQVGILHQ HNNSGFVGYL APTMREGQAY PANFPYPLIG KTAVDSITQK
 ChAd3  DYQEVGIIHQ HNNSGFVGYL APTMREGQAY PANFPYPLIG KTAVDSITQK
ChAd11  DYQEVGIIHQ HNNSGFVGYL APTMREGQAY PANFPYPLIG KTAVDSITQK
ChAd17  DYQEVGIIHQ HNNSGFVGYL APTMREGQAY PANFPYPLIG KTAVDSITQK
ChAd19  DYQEVGIIHQ HNNSGFVGYL APTMREGQAY PANFPYPLIG KTAVDSITQK
ChAd20  DYQEVGIIHQ HNNSGFVGYL APTMREGQAY PANFPYPLIG KTAVDSITQK
 hAd48  DYKAVTLPFQ HNNSGFTGYL APTMRQGQPY PANFPYPLIG QTAVPSVTQK
 ChAd4  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVTSVTQK
 ChAd5  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVASVTQK
 ChAd7  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVTSVTQK
ChAd16  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVASVTQK
  Pan6  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVASVTQK
  hAd4  DYQAVTLPYQ HNNSGFVGYL APTMRRGQPY PANYPYPLIG KSAVTSVTQK
 hAd16  DYKAVTLPYQ HNNSGFVGYL APTMRQGEPY PANYPYPLIG TTAVKSVTQK
 ChAd6  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVASVTQK
 ChAd9  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVASVTQK
ChAd10  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVASVTQK
   C68  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVTSVTQK
  Pan5  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVASVTQK
  Pan7  DYQAVTLAYQ HNNSGFVGYL APTMRQGQPY PANYPYPLIG KSAVASVTQK
 hAd41  EYQNVTLPFQ HNNSGFVGYM GPTMREGQAY PANYPYPLIG QTAVPSLTQK
 hAd40  EYQNVTLPFQ HNNSGFVGYM GPAIREGQAY PANYPYPLIG QTAVPSLTQK

        901                                                 950
 hAd12  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE
  hAd3  KFLCDRTMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE
  hAd7  KFLCDRTMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE
```

Fig. 31K

```
hAd11   KFLCDRTMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE
hAd21   KFLCDRTMWR IPFSSNFMSM GALTDLGQNL LYANSAHALD MTFEVDPMDE
hAd34   KFLCDRTMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE
hAd35   KFLCDRTMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE
  C1    KFLCDRTMWR IPFSSNFMSM GALTDLGQNL LYANSAHALD MTFEVDPMDE
 hAd1   KFLCDRTLWR IPFSSNFMSM GALTDLGQNL LYANSAHALD MTFEVDPMDE
 hAd2   KFLCDRTLWR IPFSSNFMSM GALTDLGQNL LYANSAHALD MTFEVDPMDE
 hAd5   KFLCDRTLWR IPFSSNFMSM GALTDLGQNL LYANSAHALD MTFEVDPMDE
ChAd3   KFLCDRTLWR IPFSSNFMSM GALSDLGQNL LYANSAHALD MTFEVDPMDE
ChAd11  KFLCDRTLWR IPFSSNFMSM GALTDLGQNL LYANSAHALD MTFEVDPMDE
ChAd17  KFLCDRTLWR IPFSSNFMSM GALSDLGQNL LYANSAHALD MTFEVDPMDE
ChAd19  KFLCDRTLWR IPFSSNFMSM GALTDLGQNL LYANSAHALD MTFEVDPMDE
ChAd20  KFLCDRTLWR IPFSSNFMSM GALSDLGQNL LYANSAHALD MTFEVDPMDE
 hAd48  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE
 ChAd4  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
 ChAd5  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
 ChAd7  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
ChAd16  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
  Pan6  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
  hAd4  KFICDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
 hAd16  KFLCDRTMWR IPFSSNFMSM GALTDLGQNL LYANSAHALD MTFEVDPMDE
 ChAd6  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
 ChAd9  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
ChAd10  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
  C68   KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
  Pan5  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
  Pan7  KFLCDRVMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MNFEVDPMDE
 hAd41  KFLCDRTMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE
 hAd40  KFLCDRTMWR IPFSSNFMSM GALTDLGQNM LYANSAHALD MTFEVDPMDE

        951                                              990
 hAd12  PTLLYVLFEV FDVVRIHQPH RGVIEAVYLR TPFSAGNATT
  hAd3  PTLLYLLFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
  hAd7  PTLLYLLFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
 hAd11  PTLLYLLFEV FDVVRVHQPH RGIIEAVYLR TPFSAGNATT
 hAd21  PTLLYLLFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
 hAd34  PTLLYLLFEV FDVVRVHQPH RGIIEAVYLR TPFSAGNATT
 hAd35  PTLLYLLFEV FDVVRVHQPH RGIIEAVYLR TPFSAGNATT
   C1   PTLLYLLFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
 hAd1   PTLLYVLFEV FDVVRVHQPH RGVIETVYLR TPFSAGNATT
 hAd2   PTLLYVLFEV FDVVRVHQPH RGVIETVYLR TPFSAGNATT
 hAd5   PTLLYVLFEV FDVVRVHRPH RGVIETVYLR TPFSAGNATT
ChAd3   PTLLYVLFEV FDVVRVHQPH RGVIETVYLR TPFSAGNATT
ChAd11  PTLLYVLFEV FDVVRVHQPH RGVIETVYLR TPFSAGNATT
ChAd17  PTLLYVLFEV FDVVRVHQPH RGVIETVYLR TPFSAGNATT
ChAd19  PTLLYVLFEV FDVVRVHQPH RGVIETVYLR TPFSAGNATT
ChAd20  PTLLYVLFEV FDVVRVHQPH RGVIETVYLR TPFSAGNATT
 hAd48  PTLLYLLFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
 ChAd4  STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
 ChAd5  STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGKATT
 ChAd7  STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
ChAd16  STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
  Pan6  STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
  hAd4  STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
 hAd16  PTLLSLVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
 ChAd6  STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
```

Fig. 31L

```
 ChAd9   STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
ChAd10   STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
   C68   STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
  Pan5   STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
  Pan7   STLLYVVFEV FDVVRVHQPH RGVIEAVYLR TPFSAGNATT
 hAd41   PTLLYVLFEV FDVVRIHQPH RGVIEAVYLR TPFSAGNATT
 hAd40   PTLLYVLFEV FDVVRIHQPH RGVIEAVYLR TPFSAGNATT
```

Fig. 31M

SEQ ID NO: 26
AATAAAAGATCTTTATTTTCATTAGATCTGTGTGTTGGTTTTTTGTGTG

SEQ ID NO: 27
ATGGAATTCGTTTAAACCATCATCAATAATATACCTC

SEQ ID NO: 28
CGCTGGCACTCAAGAGTGGCCTC

SEQ ID NO: 29
ATGAAGCTTGTTTAAACCCAT CATCAATAATATACCT

SEQ ID NO: 30
ATCTAGACAGCGTCCATAGCTTACCG

SEQ ID NO: 31
ATGCTACGTAGCGATCGCGTGAGTAGTGTTTGGGGGTGGGTGGG

SEQ ID NO: 32
TAGGCGCGCCGCTTCTCCTCGTTCAGGCTGGCG

SEQ ID NO: 33
GATCTAGTTAGTTTAAACGAATTCGGATCTGCGACGCG

SEQ ID NO: 34
TTCGATCATGTTTAAACGAAATTAAGAATTCGGATCC

SEQ ID NO: 35)
TATTCTGCGATCGCTGAGGTGGGTGAGTGGGCG

SEQ ID NO: 36
TAGGCGCGCCCTTAAACGGCATTTGTGGGAG

SEQ ID NO: 37
CGTCTAGAAGACCCGAGTCTTACCAGT

SEQ ID NO: 38
CGGGATCCGTTTAAACCATCATCAATAATATACCTTATT

SEQ ID NO: 39
ATGGAATTCGTTTAAACCATCATCAATAATATACCTT

SEQ ID NO: 40
ATGACGCGATCGCTGATATCCTATAATAATAAAACGCAGACTTTG

SEQ ID NO: 45
TGTCCTACCARCTCTTGCTTGA

SEQ ID NO: 46
GTGGAARGGCACGTAGCG

Fig. 32

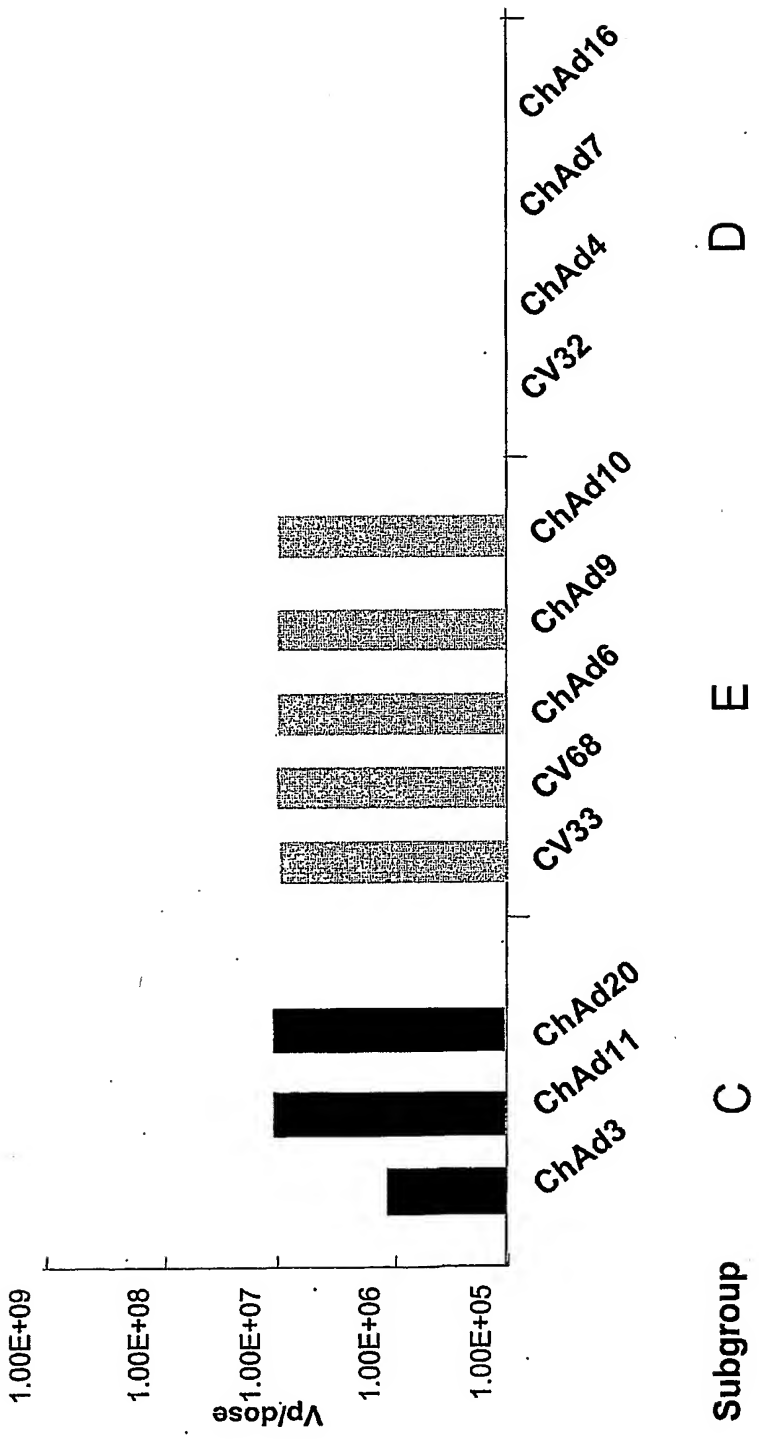

Fig. 33

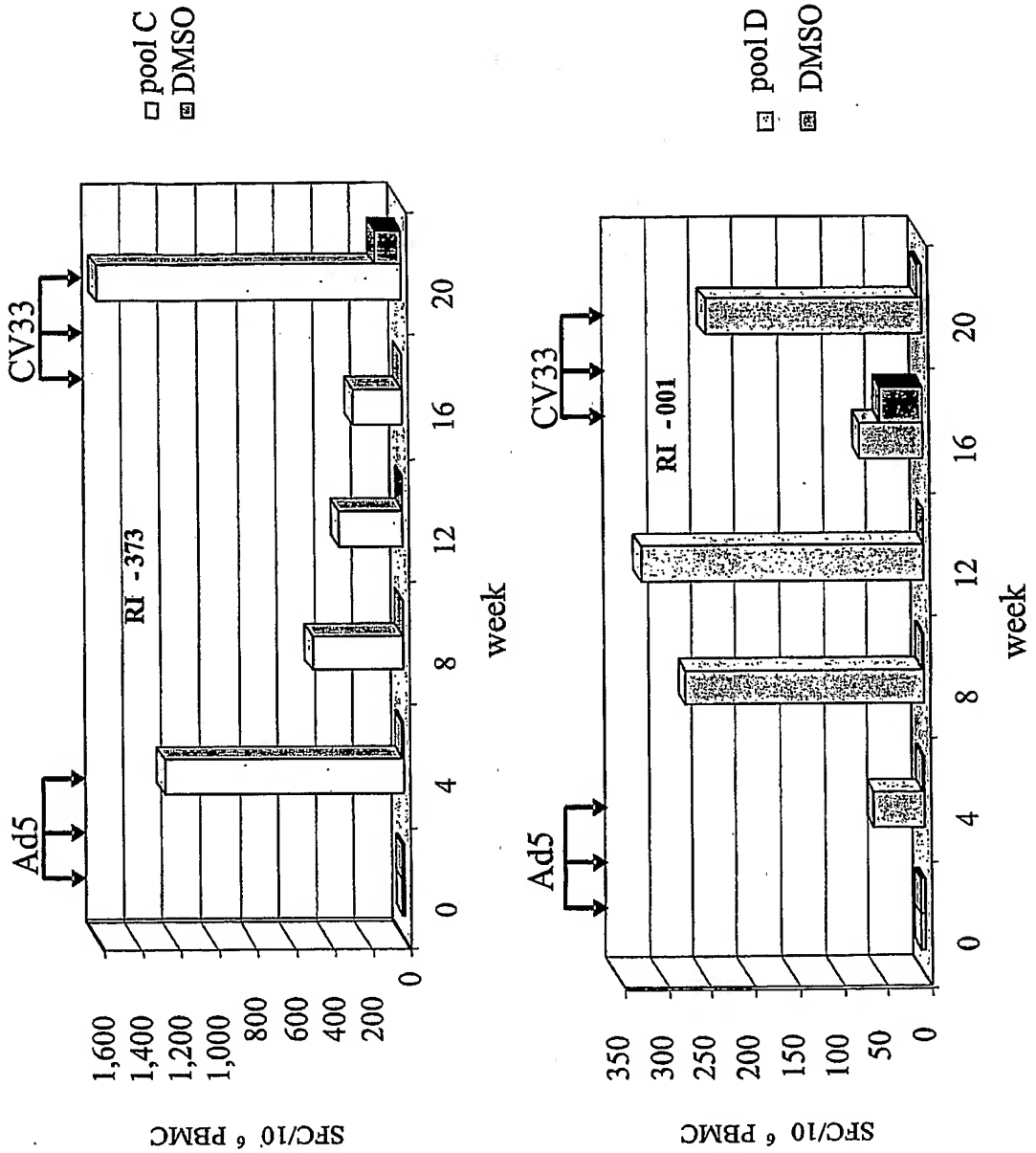

Fig. 34

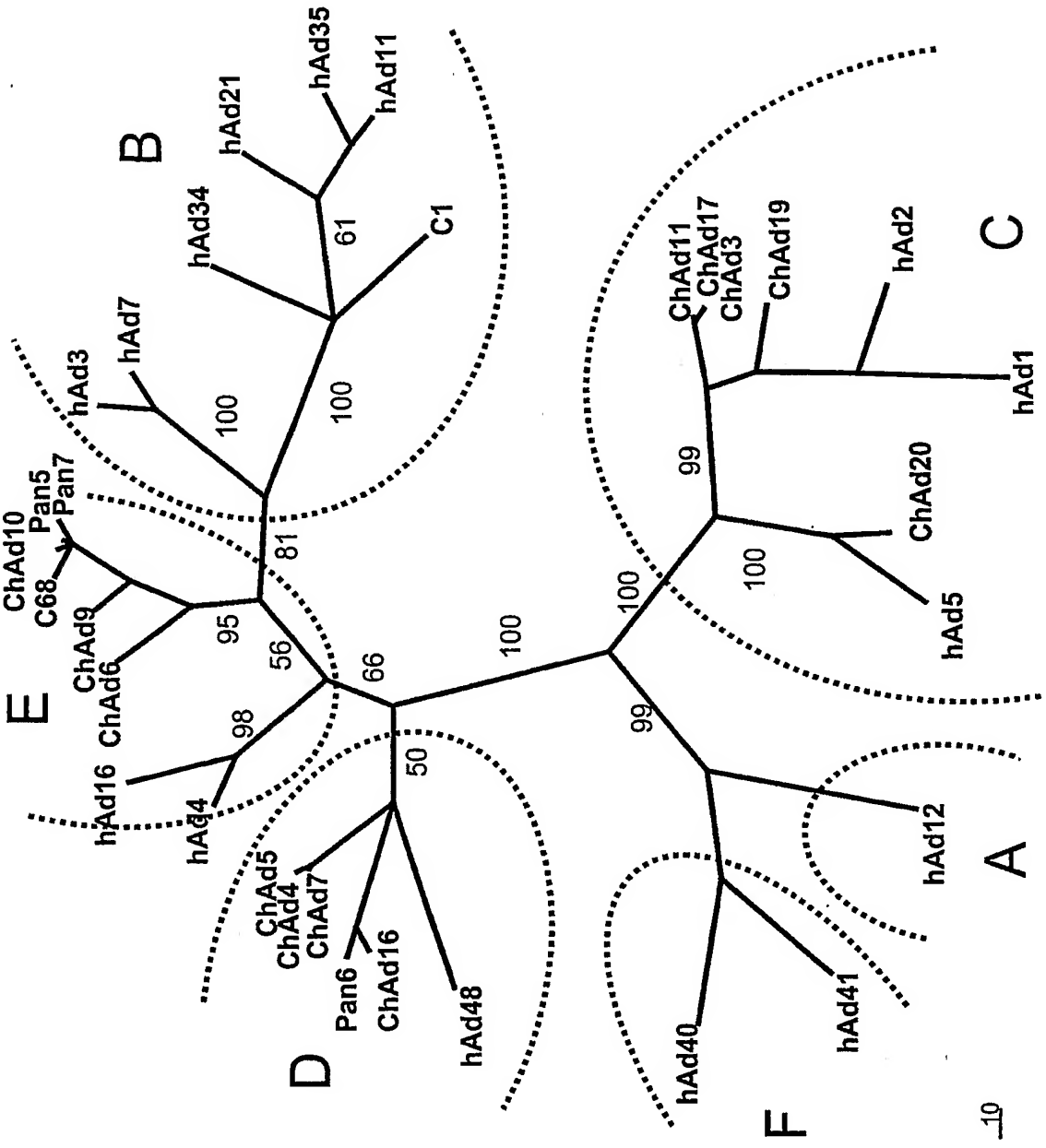

Fig. 35

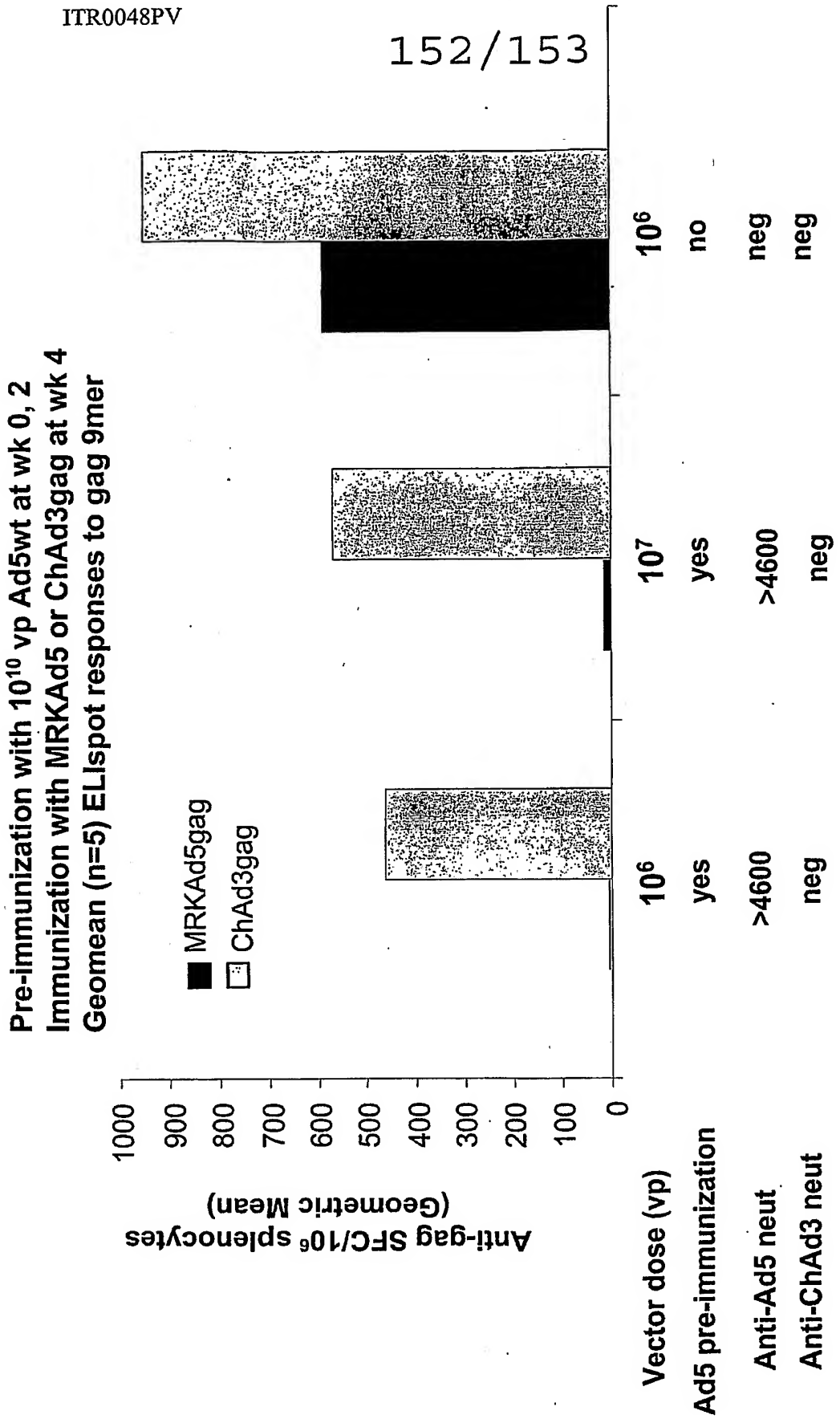

Fig. 36

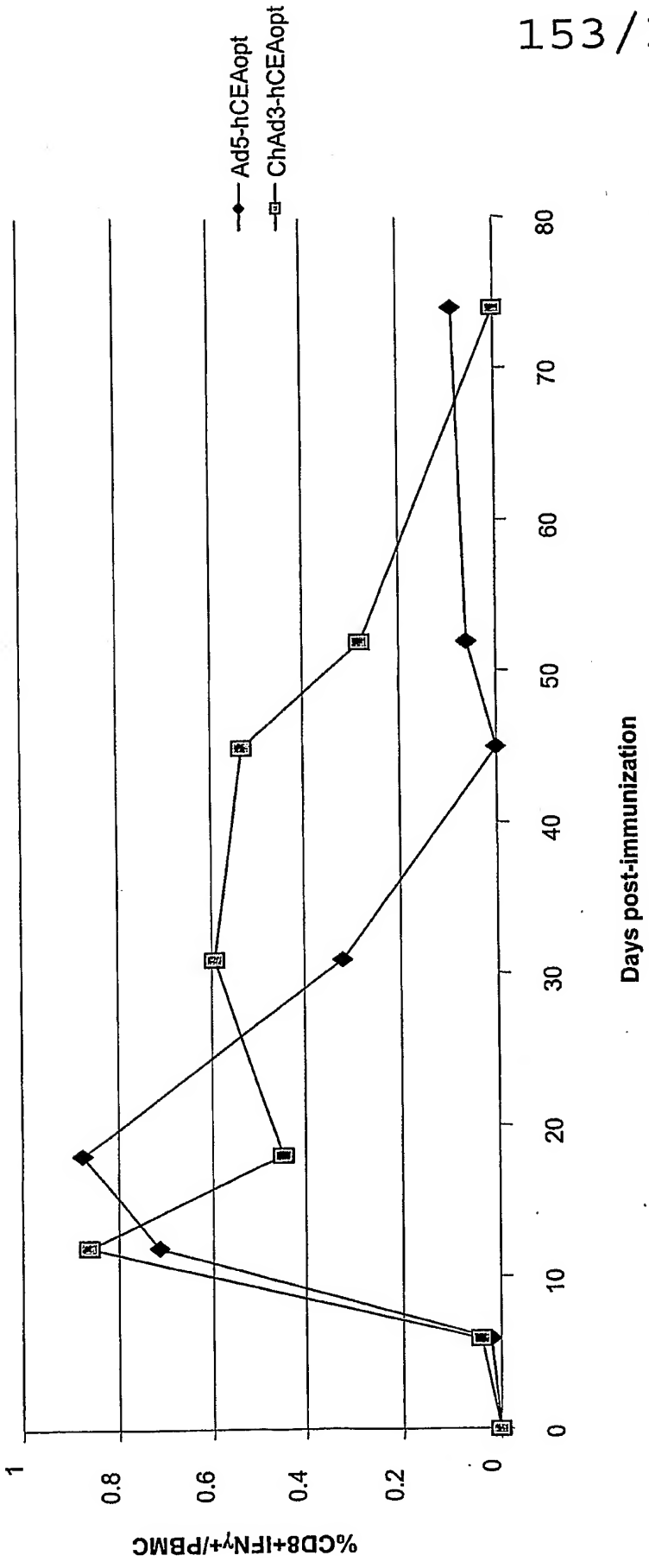

Fig. 37